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PERNICIOUS VOMITING OF PREGNANCY.[1]

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GENERAL HISTORY.

Slight degrees of nausea and vomiting in the early months of pregnancy have probably occurred from time immemorial, but according to Guéniot and Anquétin, the more severe forms of the affection were first described by Oribasius and Paul of Aegina, who, however, appeared to have no idea that it might end fatally. Similar views were held by Guillemeau, Mauriceau, and the obstetricians of the seventeenth and the greater part of the eighteenth centuries. Indeed, Dionis and many others considered vomiting a favorable sign, and thought that women subject to it were usually exempt from serious complications at the time of labor; or, as Rigby expressed it, nearly 150 years later, "a sick pregnancy is a safe one."

In 1789, Vaughan reported a case which he considered was saved from a fatal termination only by the employment of rectal feeding, so that it would seem that it was not until the latter part of the eighteenth century that it began to be recognized that vomiting of pregnancy might occasionally be so persistent as to lead to death from inanition.

As far as I can learn, Simmons in 1813 was the first to induce abortion for its relief, an example which was soon followed by Davis, Chailly-Honoré, Churchill, and others. The justifiability of the procedure, however, was first brought prominently to the attention of the profession by a discussion before the Academy of Medicine of Paris in March, 1852, when Dubois and Danyau contended that the induction of abortion was not only justifiable, but urgently demanded in severe cases, while Cazeaux held that interference was unnecessary and even hastened death in some instances.

Dubois supported his contention by his own experience in fourteen severe cases, ten of which died without operation, while abortion was induced in the other four. Only one of the latter recovered; in two others the vomiting persisted until death; while the third died from infection. Notwithstanding these apparently poor results, which he held were due to the fact that interference had been delayed so long that death was practically inevitable no matter what line of treatment was adopted, Dubois contended that abortion was the rational treatment and should be induced before the patient's condition becomes absolutely hopeless, and was urgently indicated under the following conditions:

1. When the vomiting is incessant.
2. When emaciation is rapid and the patient so weak as to be obliged to keep her bed.
3. When she faints upon the slightest exertion.
4. When pronounced alterations occur in her features.
5. When there is marked and continuous fever and an

[1] Read in Abstract before the American Gynecological Society, Buffalo, May 26, 1905.

excessive acidity of the breath, which cannot be relieved by treatment.

The next important contribution to the subject was the monograph of Guéniot in 1863, in which the author collected from the literature 118 cases of pernicious vomiting with 46 deaths, and carefully analyzed them from the point of view of etiology and treatment. Concerning the former, his conclusions were not very satisfactory, but on the other hand he taught that the induction of abortion was urgently indicated in severe cases, and should be resorted to as soon as medicinal treatment proved unavailing and the patient was perceptibly losing ground.

The work of Dubois and Guéniot greatly stimulated the interest in the subject, concerning which an immense literature gradually developed. Unfortunately the contradictory statements of the various writers have simply served to accentuate the fact that their knowledge concerning the etiology of the condition was very fragmentary and imperfect; while the manifold recommendations as to treatment indicate that they either were practically worthless, or that several types of vomiting with varying clinical histories had been grouped together in a single category.

Object of Article.

In this paper it is my object to bring together the more important contributions to the literature of the subject, and, guided by my own experience, to set up certain well defined types of the disease, in the hope of establishing more satisfactorily its etiology and laying down more definite rules for guidance in its treatment.

Leaving out of consideration all cases in which the vomiting is dependent upon conditions which have nothing to do with pregnancy, and limiting our attention only to those cases in which it is apparently due solely to the pregnancy itself or to some lesion of the generative tract—in other words adopting the distinction of Matthews Duncan between vomiting in and vomiting of pregnancy—I hope to be able to show that the evidence at present available seems to justify the differentiation of three distinct types of vomiting of pregnancy, namely: reflex, neurotic, and toxæmic, each of which is dependent upon different etiological factors and demands especial methods of treatment.

Frequency.

It is difficult to give definite figures as to the frequency of serious vomiting of pregnancy, since even the statements concerning the incidence of the ordinary morning sickness vary greatly. Thus Gardner states that the latter occurs in only 15 per cent of pregnant women, while Giles, Gerst, and Horwitz noted it in 47⅓, 66⅔, and 84 per cent of their cases respectively. My own experience leads me to believe that it is present in slightly more than one-half of all private patients. According to Pick and Lwow the pernicious type occurs about once in one thousand cases; but as their conclusions were drawn entirely from hospital experience, they do not necessarily give a correct idea as to its incidence in private practice, in which it would seem to be much more frequent. This is clearly shown by my own experience at the Johns Hopkins Hospital, where only two out of 4500 clinical cases suffered from serious vomiting of pregnancy, while I have seen ten cases during the past two years in my private and consultation practice.

It would also seem, as Horwitz first pointed out, that there is a marked variation in its incidence in different countries, as it occurs much more frequently in France, England, and America, than in Germany or Russia; a fact which may possibly be explained by the greater frequency of neurotic conditions among the inhabitants of the former countries. Indeed many competent German authorities, such as Hohl, Lomer, Frank, and Strassmann, have stated that they have never seen a case of vomiting of pregnancy end fatally; while in this country there is hardly a general practitioner of extensive experience, who has not had one or more cases in his own practice. It is likewise interesting to recall the fact that Anquétin stated that the condition had apparently become more frequent in France after the abandonment of universal venesection.

Etiology.

1. *Reflex Vomiting.*—This variety of vomiting may be due to the presence of abnormalities of the generative tract or ovum, which existed prior to the onset of pregnancy, or are coincident with it. Among such conditions may be mentioned:

(a) Abnormalities of the uterus, particularly displacements.

(b) Certain cases of endometritis.

(c) Ovarian tumors.

(d) Abnormalities of the ovum, such as hydramnios, hydatidiform mole and certain cases of twin pregnancy.

The reflex character of the vomiting of pregnancy was recognized at an early period. Mauriceau attributed it to a sympathy between the uterus and stomach, as he believed that distinct nervous connections existed between the two organs, by which abnormal stimuli originating in the diseased uterus were readily transmitted to the stomach.

That uterine displacements may occasionally be the cause of the condition is apparently demonstrated by the fact that the vomiting sometimes ceases immediately upon the replacement of a retroflexed uterus. This conception was particularly elaborated by Graily Hewitt, who published extensive monographs upon the subject in 1871, 1885, and 1888, in which he clearly demonstrated that certain cases, at least, were due to displacements of the uterus and could be cured by restoring the organ to its normal position. At the same time, he probably erred when he concluded that anteflexion had a much more deleterious influence than retroflexion.

Owing to his extensive contributions, Hewitt is generally regarded as the father of this theory, although several earlier writers held similar, but not so pronounced, views; among whom may be mentioned Busch and Moser, Stolz, Brian-Moreau, Ulrich, and others. Following the publication of

Hewitt's last monograph, his view has never lacked supporters, as is evidenced by the teachings of Guéniot in 1889 and Lwow in 1900.

From my own experience, I can state without hesitation, that in exceptional cases, a retroflexed uterus may be the exciting cause of the condition, and in such cases vomiting ceases immediately after its replacement. At the same time it must be admitted that this is not a common etiological factor, since in the vast majority of patients with retroflexion of the pregnant uterus, even when symptoms of incarceration are present, vomiting is lacking or at least no more severe than in women with perfectly normal genitalia.

Dance, in 1827, in one of the earliest autopsies performed upon a woman dying from hyperemesis, noted an abnormal thinness of the uterine wall; and since then occasional advocates have been found for the belief that the vomiting is due to undue distension of the uterus, a view which was held in part by Schroeder. While it cannot be denied that such an explanation may occasionally hold good, as is apparently demonstrated in some cases of hydramnios and twin pregnancy, it must nevertheless be admitted that it is not of universal application, and even in those cases in which it appears most probable, conclusive evidence cannot be adduced in its favor.

Horwitz, in 1883, pointed out that in certain cases the vomiting appeared to be due to inflammatory conditions of the muscular wall of the uterus, which in several of his cases was associated with peritoneal involvement. Whether these lesions were really the cause of the condition, or should be regarded merely as accidental complications, cannot be decided, though the evidence at present available makes the latter probable. Tuszkai in 1895, rehabilitated the theory of peritoneal irritation with only partial success. At the same time there can be no doubt that abnormal conditions of the uterus certainly favor the occurrence of vomiting.

The uterine origin of vomiting was likewise advocated by Martin in 1904, who stated that the majority of cases should be attributed to hyperæmia of the uterus and its impaction in the pelvic cavity; while Evans of Montreal taught that the ordinary morning sickness was probably connected with the rythmical contractions of the organ.

In 1849, J. H. Bennett in his work on inflammation of the uterus directed attention to the part which he believed was played by inflammatory conditions of the cervix in the production of the vomiting of pregnancy, and ever since then this view has had numerous adherents; and he himself, in 1875, stated that more extended experience had only served to confirm his original views.

A little later Copeman invoked the influence of the cervix in another manner and assumed that the vomiting was due to an irritation resulting from its abnormal rigidity, particularly in the region of the internal os, and held that the vomiting could be cured by dilating the cervix. This view and the procedure dependent upon it was accepted by Rosenthal and many others and enjoyed considerable vogue for some years, but has gradually fallen into disrepute; although even as late as 1896, Kehrer reported a case which he considered demonstrated the correctness of such teachings. Cervical catarrh has likewise been considered to play an important etiological part, and Lwow stated that 75 per cent of the women suffering from vomiting of pregnancy presented this abnormality.

As far as I am able to ascertain, the causal relation between abnormalities of the cervix and the more severe forms of vomiting has not been conclusively demonstrated, nor do I think that it will be in the future; as it seems to me that a palpably accidental condition has been erroneously considered as causal. This contention is well exemplified by a case of Davis, in which several small cysts in the cervix were considered as the etiological factor; while autopsy showed marked lesions in the liver and kidneys; and still more forcibly by a case of Lang in which inflammation of the cervix was considered the essential factor, while autopsy demonstrated the presence of acute yellow atrophy of the liver.

Ever since 1827, when Dance at autopsy upon a patient dying from vomiting of pregnancy, found suppurative changes in the decidua, it has been considered that endometritis may play an important part in the production of the condition, a view which in modern times has been particularly insisted upon by Veit, Jaffé, Jaggard, Flaischlen, Goldspohn, and many others. Nevertheless it does not appear that its advocates have adduced conclusive evidence in its support, and it seems probable that endometritis when it occurs, should generally be regarded as an accidental complication, rather than an important etiological factor. At the same time it must be admitted that it may tend to exaggerate what might otherwise be only a minor complaint.

There can be no doubt that in exceptional instances the presence of tumors of the ovaries may accentuate or even cause serious vomiting. Such a connection was clearly demonstrated in a case of Krassowsky's, in which very severe vomiting ceased immediately after the removal of a small ovarian tumor, and in one of my own cases a similar result followed the removal of a small fibro-myoma of the ovary.

Clinical observation apparently shows that both hydramnios and twin pregnancies predispose to excessive vomiting, though whether this is the result of the mere overdistension of the uterus, or whether it is associated with some toxæmic condition has not yet been demonstrated.

Hydatidiform mole has a similar effect, and Bué has reported three cases in which the vomiting ceased immediately after the evacuation of the mole, and has collected a large number of similar cases from the literature. Likewise, in one of my cases the spontaneous expulsion of the mole prevented the induction of abortion for the relief of vomiting. But in this condition, as well as in twin pregnancy and hydramnios, the exact interpretation of the effect of the abnormality is not easy; as it is possible, on the one hand, that the vomiting may be merely the result of over-distension of the uterus, while on the other, it may quite as readily be attributed

to a toxæmic condition, which may be due to abnormal metabolism on the part of the mother or fœtus, or to the formation of syncytiotoxins resulting from the presence of unusually large amounts of fœtal elements in the maternal blood. The latter conception has been particularly elaborated by Veit and Behm and will be considered in detail under Toxæmic Vomiting.

Chorio-epithelioma has likewise been invoked as a cause of the condition by Davis and Harris, although in their case it is questionable whether the vomiting was due to the presence of fœtal tissues in the growth itself, or merely to the mechanical action of the metastases which were found in the brain at autopsy.

2. *Neurotic Vomiting.*—Although the effect of pregnancy upon the mental, moral, and nervous equilibrium had long been recognized, and Anquétin, Tisserand, Duncan, Rosenthal, Ahlfeld, and others had pointed out that many cases of severe vomiting were neurotic or hysterical in origin, it was nevertheless not until Kaltenbach read his paper before the Berlin Obstetrical Society in 1890, that general attention was directed to this phase of the subject.

On that occasion he pointed out the necessity for narrowing the conception of the pernicious vomiting of pregnancy and confining it strictly to those cases in which there was no disease of other organs or of the generative tract to which it might be attributed. At the same time he emphasized the great paucity of positive autopsy findings, and commented upon the contradictory character of the lesions noted.

In this restricted sense, he held that the severe cases of hyperemesis were the result of an abnormal condition of the nervous system by which the reflex irritability was heightened and the reflex control lessened. This being the case, it could readily be understood how the irritation might be increased by diseased conditions on the part of the generative tract on the one hand or of the stomach on the other. Accordingly, he concluded that the vast majority of cases of vomiting of pregnancy were due to a neurosis, more or less allied to hysteria; although he was compelled to admit that many of the patients presented no evident manifestations of the latter condition. He therefore assumed that in many instances a hysteria, which had previously been larval, might become manifest under the influence of pregnancy. In view of its neurotic nature, he insisted upon the value of suggestion and the rest cure in its treatment, and held that if they were intelligently carried out, the field for the induction of abortion would be greatly limited, if not entirely obliterated.

This paper immediately gave rise to considerable discussion, and a number of authors, among whom may be mentioned Ahlfeld, Chazan, Rosenfeld, and others, claimed that they had antedated Kaltenbach's views by a number of years. As has already been indicated, this was undoubtedly true; but nevertheless it would seem that the credit rightly belongs to Kaltenbach, as he was the first to insist upon the importance of neurotic influences in their entirety. In this connection, it is interesting to note that two years later Mettler of Chicago, enunciated almost identical views, apparently without knowledge of Kaltenbach's work.

The neurotic origin of the condition was enthusiastically accepted by a number of writers, among whom may be mentioned Luez, Klein, and Graefe. Klein published histories of a number of cases and insisted upon the curative value of an absolute rest cure and attached less importance to the action of suggestion. He stated that the vast majority of cases could be promptly cured by putting the patient to bed, keeping her absolutely quiet, prohibiting all intercourse with her family and friends, and at the same time administering small quantities of iced milk at frequent intervals, and if this was not well borne to resort entirely to rectal feeding. If, however, such a course did not lead to the desired result within three or four days, he advocated the removal of the patient to a well regulated hospital, where she could be placed under ideal conditions for a very strictly conducted rest cure. Graefe expressed similar views in his original article in 1900 and reiterated them more strongly in 1904.

To anyone who has had considerable experience with this class of cases there can be no doubt that in many the vomiting must be attributed to some neurotic condition, as is manifested by the remarkable cures which sometimes follow all sorts of unphysiological procedures, as well as the mere threat to induce abortion, or a feigned attempt to bring it about. Only upon such a hypothesis can one explain the results obtained by Muret, Damany, and others. Thus the former observed a patient who had lost 49 pounds in weight as the result of incessant vomiting, which ceased immediately upon a single lavage of the stomach. In Damany's case equally satisfactory results were obtained by the use of an electrical battery, which was later found to be entirely out of order. Moreover, it is more than probable that the vast majority of cures following the application of leeches to the epigastrium or cervix, the dilatation of the latter by Copeman's maneuver, or the application of various drugs are susceptible of a similar explanation.

At the same time it should be borne in mind that it is possible that the underlying cause of the neurosis may be a mild toxæmia, but at present satisfactory evidence cannot be adduced in support of such a view.

When Graefe's first paper was read before the Leipzig Obstetrical Society in 1900, Winscheid stated in the discussion that the tendency to attribute all cases to neurasthenia or hysteria was too extreme, as he did not believe that such conditions could give rise to the extreme emaciation and cachexia which characterized the severe cases. To my mind, however, this objection does not necessarily hold good, as I have in several instances seen women, who had become markedly emaciated and were apparently dying from starvation, immediately cease vomiting after a vigorous lecture or upon the threat of inducing abortion, after I had unduly magnified its dangers.

3. *Toxæmic Vomiting.*—According to Mauriceau, one of the earliest theories concerning the production of the vomiting

of pregnancy was that it was due to the excretion by the stomach of humours resulting from the suppression of the menstrual function. As far as I have been able to ascertain, Fischl in 1884, was the first modern writer to suggest the toxæmic nature of the condition, being led to this conclusion after observing a woman, admitted to the hospital in a torpid condition with slight fever with a history of severe continuous vomiting, who was immediately cured by the evacuation of a densely impacted colon. As the result of his experience, he stated that the vomiting of pregnancy might be either essential or symptomatic, and held that the former would become more and more rare as the cases were more carefully investigated.

The following year (1885), Jolly reported two cases of paralysis which occurred in pregnant women suffering from the vomiting of pregnancy, and attributed the former condition to a neuritis which was probably caused by some toxic substance peculiar to pregnancy. Similar cases were soon described by Moebius, Whitfield, Desnos, Joffroy, and Pinard, and others, who expressed a similar belief concerning the inter-relation of the two conditions, but did not adduce absolute proof as to its correctness.

In 1892, Lindemann reported the autopsy findings upon a patient of Solowieff's, who died from multiple neuritis complicating hyperemesis, and stated that there were histological signs of parenchymatous neuritis as well as fatty degeneration and cloudy swelling of the liver and kidneys. As he found similar lesions in the organs of the fœtus, he was inclined to believe that he had adduced direct proof of the toxæmic nature of the condition, as the presence of lesions in both the mother and the fœtus could be due only to the circulation of some toxic substance.

Following Lindemann, a considerable number of cases of neuritis associated with vomiting were reported by Eulenberg, Stembo, Mader, Kühne, Kreutzmann, Bar, and others. Eulenberg gave a tabulated list of the cases occurring up to the time of his report, but thus far no one has advanced irrefutable proof in favor of the toxic nature of the two conditions, although each succeeding observation has rendered it more probable.

Additional support in favor of the toxæmic nature of the vomiting of pregnancy is afforded by its occasional association with jaundice. As early as 1879, Matthews Duncan suggested that the underlying factor in certain of the fatal cases, at least, was acute yellow atrophy of the liver, and supported his contention by autopsy in one case. This view was likewise advocated by Roughton in 1885, but obtained little if any recognition; although it is interesting to note that Lomer in his article upon icterus in pregnancy likewise suggested that possibly some connection existed between hepatic disturbance and the production of vomiting.

The toxæmic theory was likewise advocated in a modified form by Holladay who, in 1886, suggested that when the vomiting persisted after the fourth month of pregnancy it was probably due to the action of the secretion of an abnormally persistent corpus luteum.

Following these suggestions, there was a lull in the advocacy of the toxæmic nature of the condition, and it was not until the last years of the 19th century that other writers began to insist upon its possibility, when Allbutt and Bacon, in 1896 and 1897 respectively, expressed themselves in its favor upon purely theoretical considerations.

In 1898, Bouffe de Saint-Blaise in a long article upon the auto-intoxication of pregnancy, which was based in great part upon Pinard's hepato-toxæmia theory, made a tolerably clear case for eclampsia and the pre-eclamptic toxæmia; but when he attempted to apply the theory to the other complications of pregnancy the outcome was much less satisfactory.

With the exception of the positive autopsy findings of Lindemann, and several isolated cases of acute yellow atrophy of the liver, it was not until 1901 that Champetier de Ribes and Bouffe de Saint-Blaise reported definite hepatic lesions in vomiting of pregnancy. In a communication to the Society of Gynecology, Obstetrics and Pædiatrics of Paris, they briefly described the autopsy findings in a woman dying in convulsions at the end of pregnancy, who had suffered from vomiting throughout its entire course, and reported the presence of lesions in the liver which they considered identical with those observed in eclampsia, and therefore concluded that the anatomical substratum was the same in both conditions. Unfortunately the promised report of the microscopical examination of their specimens has not yet appeared.

Since then an abundant literature has developed concerning the toxæmic nature of the condition, and four main theories have been advanced as to the source of the toxic materials giving rise to it:

A. Gastro-intestinal tract;
B. The ovum and its appendages;
C. Ovarian secretion;
D. Hepatic lesions.

A. Intestinal Origin.—The most consistent advocate of the intestinal origin of the condition is Dirmoser, who in 1901 summed up his observations in a monograph and two years later reiterated his experience in another article. He pointed out that in women suffering from the vomiting of pregnancy examination of the urine showed an increased amount of uric acid, indoxyl, skatoxyl, aromatic sulphates, phenols and nucleo-albumins; while the following abnormal substances were frequently noted—acetone, diacetic acid, peptone, urobilin, etc. From these observations he concluded that one had to deal with the absorption of toxic materials derived from the decomposition of carbo-hydrates in the stomach and proteids in the intestinal tract, which circulating in the blood brought about the neurosis, which, in turn, caused the vomiting. Moreover, he believed that the results of treatment still further substantiated this view, in that the administration of intestinal antiseptics and the copious employment of rectal irrigation frequently led to cure, or at least to a marked improvement in the condition of the patient. In his article of

1903, he added another link to his chain of evidence by demonstrating that the intestinal contents of such patients were more toxic than in normal individuals, as indicated by the fact that their administration to mice and rabbits was promptly followed by death, while control experiments gave negative results.

B. Fœtal Origin.—In 1902 and 1903 Veit, taking advantage of the fact that portions of the periphery of the ovum-chorionic epithelium and even portions of the villi are constantly gaining access to the maternal circulation during pregnancy, enunciated an hypothesis along the line of Ehrlich's side chain theory, which he believed capable of affording a satisfactory explanation for most of the abnormalities of pregnancy. He held that under normal conditions, the fœtal products gaining access to the maternal blood were readily rendered innocuous, but that when excessive amounts were introduced Nature was no longer able to fulfill her task and consequently cytotoxins were developed, which brought about lesions in the maternal organs and likewise led to hæmolytic changes in the blood.

Veit attempted to demonstrate the correctness of his theory by injecting into rabbits varying quantities of an emulsion of human placentæ; and, upon finding degenerative changes in the kidneys and the presence of albumin in the urine, contended that his point was proven. His conclusions naturally evoked the greatest interest, and similar experiments were promptly undertaken by Weichardt, Leipmann, Wormser, and others, with the result that considerable discredit was cast upon the syncytio-toxin theory. At present the general consensus of opinion seems to be that Veit's conclusions were based upon imperfect methods of experimentation, and that equally positive results would have followed the introduction of beefsteak or any other heterogeneous animal material. At the same time there is no doubt concerning the almost universal occurrence of "placental deportation," and accordingly it would seem rash to conclude that it may not give rise to abnormal conditions in some instances; but at the present time it would seem inadvisable to accept Veit's theory until further experimental contributions conducted along proper lines demonstrate its correctness.

Veit's theory has received a certain amount of support from the observation of hæmoglobinæmia and hæmoglobinuria associated with the jaundice and vomiting of pregnancy by Hirschberg, Schaeffer, Fellner, Brauer, von der Velden, and others. And it must be admitted in all such cases that the abnormal condition of the blood must be due to the action of some hæmolytic agent; but whether this is derived from fœtal cells or from other sources has not as yet been determined.

Shortly afterwards Behm reported to the Berlin Obstetrical Society that he had obtained excellent results in several cases of hyperemesis by the employment of abundant rectal injections of salt solution, and held that his results clearly indicated the toxic origin of the vomiting. He accepted Veit's syncytiotoxic theory in its entirety, and stated that the beneficial results following the use of saline solutions could be readily explained by supposing that it served to wash out of the system the toxic agents which were produced after the entrance of abnormal amounts of fœtal tissue into the maternal blood.

While there can be no doubt as to the correctness of Behm's actual observations, the objections which have already been made to the acceptance of Veit's theory can be urged still more strongly against the theoretical deductions of the former. Moreover, it is interesting to note that the use of salt infusions in this connection was not original, as they had been employed by Condamin for many years prior to the appearance of Behm's communication. Following the teaching of Veit and Behm, not a few authors, among whom may be mentioned Clivio, Jardine and Kehrer have adopted more or less similar views.

C. Ovarian Origin.—Reference has already been made to the views of Holladay concerning the part played by the secretion of abnormal corpora lutea in the production of vomiting in the latter months of pregnancy. Pierrehughes in 1902, after carefully studying 6 cases, concluded that it was more than probable that in many cases, at least, the vomiting of pregnancy was due to some abnormality in the ovarian secretion. His argumentation was not at all conclusive and would apply equally well to abnormal products from the thyroid, liver, or other organs. It is interesting to note, however, that his conclusions were based in part upon metabolic observations by Meillère, who demonstrated in all his cases a decrease in the amount of chlorides in the urine and a diminished urea coefficient.

At the same time, Pierrehughes and Meillère made the interesting observation that while the amount of urea was found to be diminished when determined by accurate chemical methods, the urine nevertheless decomposed an amount of sodium hypobromite sufficiently large to indicate the presence of a normal urea content. The practical bearing of this observation will be dwelt upon when we consider the differential diagnosis of the several varieties of vomiting.

Somewhat similar views were advanced by Turenne in 1905, who held that the less severe types of vomiting were due to the suppression of the ovarian secretion during pregnancy, and that the condition might be alleviated or cured by supplying the deficiency by the administration of ovarian extract or tablets. He reported 24 cases in which excellent results were obtained by this means.

D. Hepatic Origin.—Reference has already been made to the views expressed by Matthews Duncan, Roughton, and Lomer concerning the possible part played by the liver in the production of vomiting, as well as to the autopsy findings of Lindemann, Champetier de Ribes and Bouffe de Saint-Blaise. The hepatic origin of the condition, however, was first brought prominently forward by Stone in 1903, who reported the autopsy findings in a fatal case of vomiting, in which the liver presented the lesions of acute yellow atrophy, in that the entire central portion of each lobule had undergone complete

necrosis, while the peripheral portion showed signs of fatty degeneration, and only a few cells remained perfectly normal.

Stone's observations were confirmed by Ewing, who within the past few months reported finding similar changes in the livers of four women dying from the vomiting of pregnancy, one of whom had a convulsion immediately before death. As the result of his experience, Ewing concludes that both vomiting of pregnancy and eclampsia are closely allied conditions and are associated with similar hepatic lesions, and therefore should be grouped together under a common heading —toxæmia of pregnancy.

Edgar has advanced similar views, which are based upon Ewing's findings and not upon personal observation.

While there can be no doubt as to the correctness of the observations of Stone and Ewing concerning the association of lesions characteristic of acute yellow atrophy of the liver with certain cases of vomiting of pregnancy, I cannot accept their conclusions as to the identity of eclampsia and vomiting, as will be brought out more fully further on.

My own experience with the toxic type of vomiting of pregnancy dates from May, 1903, when I lost a patient after the induction of abortion at the 3d month. (Case I at end of article.) At the time the operation was undertaken her condition was fairly satisfactory and gave fair promise of a successful outcome. The operation itself was not difficult, and immediately after its completion the vomiting ceased for eighteen hours, after which the patient began to eject at frequent intervals, large quantities of dark, coffee-ground like material without apparent effort. She gradualy passed into a torpid condition and later became comatose and died fifty-four hours after the abortion.

At the autopsy, which I was fortunate enough to obtain, we found changes in the liver, identical with those observed by Stone and Ewing, associated with intense degeneration of the secretory portion of the kidneys. (Fig. 1.)

This case made a deep impression upon me, as the patient clearly seemed to succumb to an intoxication rather than to starvation as is usually stated. But at that time I did not fully appreciate the significance of the hepatic lesions, for whose production I attempted to account by invoking one of the more common explanations, and, finding none, was inclined to regard it merely as an accidental complication.

Further experience, however, soon led me to change my opinion, for within the next year, I saw five other cases of severe vomiting of pregnancy, in all of which I felt compelled to resort to the induction of abortion. Two patients died, one just as the case mentioned above, and the other at the 7th month with the clinical symptoms characteristic of acute yellow atrophy. The remaining three patients were seriously ill, but recovered. Unfortunately, I was unable to obtain an autopsy in the fatal cases, but in two of the cases which recovered (Cases 2 and 3), I was able to make accurate metabolic observations, both before and after the induction of abortion. The results obtained were so surprising as to place the matter in an entirely new light and to force me to conclude that the hepatic changes certainly played a most prominent part in the fatal issue. Since then I have had an opportunity to observe a fourth toxæmic case, as well as several neurotic ones, in which accurate metabolic observations were made, and which served to confirm me more fully in the view just mentioned.

In the three toxæmic cases (2, 3, and 4) in which careful metabolic observations were made, I found that the total nitrogen output was practically normal, while the urea nitrogen was considerably diminished, and the amount of nitrogen excreted as ammonia greatly increased, so that the so-called ammonia coefficient, instead of representing 3 to 5 per cent of the total nitrogen of the urine, reached 32, 38, and 46 per cent respectively. This condition clearly indicated a marked disturbance in metabolism and can readily be brought into relationship with the hepatic changes.[1]

Since observing my case of acute yellow atrophy of the liver accompanying hyperemesis, I have carefully searched the literature for similar observations and have found the following autopsy reports: one case each reported by Duncan, Roughton, Hirschberg, Lang, Beatty, Stone, Zaborski and four cases by Ewing, which together with my own make a total of twelve observations. Moreover, in five other cases reported respectively by Schmorl, Erismann, Lindemann, Davis, and Zaborski, marked fatty degeneration of the liver and kidneys was noted.

When one contrasts the extremely contradictory results obtained at autopsy upon women dying from the vomiting of pregnancy with the uniformity of the lesions observed in the seventeen cases just mentioned, one cannot fail to suspect that the association between the two conditions cannot be merely accidental, but that they must bear some direct connection to one another. Likewise, it seems very probable to me that many similar cases must have been overlooked in the past, for the reason that the majority of the autopsies were not performed in hospitals, but in private houses, and frequently by persons little skilled in pathological technique, and who, while searching diligently for lesions of the generative or intestinal tract, would very likely overlook so unexpected a change in the liver.

Moreover, when one studies the clinical history of acute yellow atrophy one cannot fail to be impressed with the marked relationship which it and the allied states of icterus gravis, typhoid icterus, etc., bear to pregnancy. According to Lebert, Kerkring in 1706 was the first to report the death of a pregnant woman from icterus gravis, and since that time everyone who has studied the condition has laid stress upon the association, as is indicated by the writings of Horaczek, Ozanam, Budd, Rokitansky and all subsequent investigators. Thus, Thierfelder stated that 62 per cent of the 143 cases which he collected from the literature affected pregnant women; while Quincke estimates that more than 60 per

[1] Since writing the above I have observed three additional cases, with the same urinary findings. In each instance recovery promptly followed the induction of abortion.

cent of all cases occur in women, a majority of whom are pregnant.

Of course it is well known that ordinary acute yellow atrophy of the liver usually occurs in the second half of pregnancy and particularly after the 7th month; while the fatal cases of vomiting of pregnancy are much more common in the first half of gestation. At the same time, however, exceptions occur in both directions, Beatty and Le Masson having reported cases of acute yellow atrophy at the 6th and 8th weeks respectively; while occasional deaths result from vomiting in the second half of pregnancy. If it should eventually be demonstrated that toxæmic vomiting and acute yellow atrophy are really manifestations of similar toxic processes, it would seem difficult to explain their varying behaviour.

From our knowledge of the liver, it would seem that it is in a state of particular susceptibility during pregnancy, when it is much more prone to abnormal processes than at other times. Thus, Tarnier in his graduation thesis in 1857 stated that fatty degeneration of the liver was a usual concomitant of pregnancy and his contention was confirmed by Blot. Unfortunately these observations were made upon women dying from puerperal infection, and as similar observations upon normal pregnant women made in recent years are not at hand, it must remain doubtful for the present whether this condition of the liver is a characteristic accompaniment of pregnancy or merely a sequel of fatal puerperal infection.

At the same time there is no doubt that the liver in pregnancy offers a locus minoris resistentiae, as is clearly shown by the occurrence of epidemics of catarrhal jaundice at that time. Thus, within the past one hundred years numerous such epidemics have been reported in which large numbers of the inhabitants in certain localities were affected. Under such circumstances the disease ran its ordinary course in men and in non-pregnant women; whereas in pregnant women it was remarkably fatal, as more than one-half the pregnancies ended in abortion or premature labor and many of the women died in coma and occasionally in convulsions. The most important of these epidemics were reported by Kercksig in Ludenscheid, 1794; Charpentier in Rubaix, 1854; Bardinet in Limoges, 1859; Saint Vel in Martinique, 1861; Meunier in Paris, 1871; Smith in St. Paul, Minnesota, 1873; Klingelhoefer in Heusenstamm, 1876 and Young in 1898.

In this connection it is interesting to recall the fact that pregnancy itself sometimes appears to be the etiological factor concerned in the production of the jaundice, as is well illustrated by the fact that certain individuals suffer with jaundice in each pregnancy. Such cases have been reported by Beking, Benedict, Schaeffer, Brauer, van der Velden, and others. In several instances it recurred in from four to six successive pregnancies, and was frequently associated with hæmoglobinæmia and hæmoglobinuria. In Benedict's case the same tendency was noted in two sisters.

Moreover, it should be borne in mind that other functions of the liver are more or less seriously interfered with during pregnancy. Thus, Payer has pointed out that alimentary glycosuria is readily produced in 80 per cent of all pregnant women. And the investigations of Strauss have shown that the ease with which such a condition can be produced in non-pregnant individuals affords a valuable index as to the degree of hepatic insufficiency. Likewise, Charrin and Guillement have demonstrated that the liver cells of pregnant guinea pigs contain an unusually large amount of glycogen, thereby apparently indicating that less of it is consumed during pregnancy than at other times. They consider that such a condition renders more difficult the storing of additional quantities of glycogen, so that a considerable portion of the sugar ingested is promptly eliminated, instead of being converted into glycogen and stored for future use. If their supposition proves correct, it would afford a satisfactory explanation for the production of alimentary glycosuria.

When one attempts to explain the significance of the changes in metabolism noted in my toxæmic cases, one finds that it is difficult to do so satisfactorily. Ever since Schmiedeberg and Schroeder pointed out that ammonia was a forerunner of urea and was converted into it in the liver, it has been assumed that any condition which interferes with complete oxidation would tend to bring about an increase in the amount of ammonia excreted and a corresponding decrease in the urea output. Minkowski went a little further and showed that the actual precursor of urea was ammonium carbamate, which by oxidation was readily converted into urea. At first glance it would therefore seem permissible to suppose that the necrotic lesions observed in the liver might interfere with the complete oxidation of nitrogenous materials and thus lead to a marked increase in the ammonia coefficient at the expense of the urea. Moreover, such a conclusion would apparently harmonize with the urinary findings in acute yellow atrophy of the liver and acute phosphorus poisoning; since in both conditions there is marked destruction of liver tissue, associated with a considerable increase in the ammonia coefficient, though according to Neuberg and Richter, the latter does not reach so high a figure as in the cases of vomiting studied by me.

On the other hand it is probable that the relation between the liver changes and the high ammonia coefficient is not so direct, and that the increased ammonia output is not necessarily a manifestation of the destruction of liver tissue, but rather indicates that an excessive amount of acid material has been set free in the circulation and whose neutralization is absolutely essential if life is to continue. Thus, Münzer believes that such an explanation holds good for both acute yellow atrophy and phosphorus poisoning and, reasoning by analogy, there is no inherent reason why it should not apply to certain cases of toxæmic vomiting of pregnancy as well. Unfortunately it is extremely difficult at present to formulate a well defined expression of opinion in this regard, as the entire doctrine of acid intoxication seems to be still sub judice. Thus, while diabetes is considered the classical example of intoxication with oxy-butyric acid, and the increased ammonia coefficient accompanying it merely a manifestation

of an attempt to neutralize it, it must nevertheless be admitted that our knowledge of the ultimate factors concerned in the excessive production of the acid is still very fragmentary.

Another example of excessive ammonia output is found in certain cases of gastro-enteritis in children, to which Czerny and Keller directed attention in 1897. They pointed out that in such cases the ammonia coefficient frequently rose as high as 30 to 52 per cent, and were in doubt whether it was a manifestation of an acid intoxication or was directly due to some disturbance in the function of the liver, probably resulting from absorption of toxic material from the intestines. Pfaundler on the other hand contended that neither view was correct, and held that the high ammonia output was attributable almost entirely to the presence of excessive amounts of fat in the food, which was decomposed in the intestines into its component acids, which were readily absorbed and required prompt neutralization. Plausibility is lent to his contention by the fact that the ammonia coefficient can be promptly lowered by simply decreasing the amount of fat taken with the food.

Moreover, Schittenhelm has shown that in adults a considerable increase in the ammonia coefficient may be brought about by arbitrary variations in the character of the diet and by other artificial conditions. Thus, he observed that an increase in the amount of fat ingested, or the administration of dilute hydrochloric acid, would readily bring about such a condition, which would promptly disappear upon the administration of an alkali, or a change in the character of the food. Moreover, he showed very clearly that various abnormal conditions of the liver were likely to lead to a similar change, and considered that variations in the ammonia coefficient of the urine might afford a fairly reliable index of the extent to which the hepatic function had become impaired.

That the absorption of toxic materials from the intestines may lead to changes in the ammonia output was shown by the experiments of Glaessner. This investigator, finding that none of the usual methods brought about prolonged constipation in dogs, exsected a portion of the intestine and replaced it in the reverse direction, so that its peristaltic movements were opposed to those of the rest of the bowel. This operation had the desired effect and the dog remained constipated for ten days to two weeks, at the end of which time an abundant stool would be passed, to be followed by another period of constipation. Careful study showed that the metabolism was of the ordinary type immediately following evacuation of the bowels, whereas the ammonia coefficient increased to double its usual value as the constipation became more marked.

To still further complicate the interpretation of the matter, Folin and Möner have shown that in individuals obtaining an insufficient amount of food, or who are actually starving, there is a marked increase in the ammonia coefficient, which in the cases studied by them reached 26.79 and 40 per cent respectively. Moreover, the former investigator showed that the substitution of a purely vegetable for a mixed diet was attended by a marked decrease in the urea and an increase in the ammonia coefficient, while some of the nitrogenous substances, such as kreatinin, underwent a still more marked distortion.

From the considerations just adduced, it would therefore seem evident that an increase in the ammonia coefficient may or may not afford conclusive evidence of the existence of an acid intoxication, and that in the present state of our knowledge, it would be inadvisable to dogmatise too strongly concerning its significance. This is particularly the case in my own observations, as acetone, diacetic, oxy-butyric acid, and allied substances were not found in the urine, and leucin and tyrosin were likewise absent in the two cases in which they were searched for. I did not attempt to determine the alkalinity of the blood, although it is hardly likely that notable changes would have been detected, even though an underlying acid intoxication were present, since an excess of acid would immediately have been neutralized by an increased production of ammonia and thus withdrawn itself from observation.

However, it seems to me that even had we been able to determine the presence of abnormal acids in the urine, the existence of an acid intoxication would not necessarily have been demonstrated, and while we might seriously consider its possibility we should nevertheless have been unable to advance a satisfactory explanation for its production. This being the case, I feel at present that I must remain content with demonstrating that in certain cases of toxæmic vomiting of pregnancy there is a marked disturbance in metabolism, which is manifested by a great increase in the ammonia coefficient, and that it must be left to future investigations to determine whether the change is directly due to the inability of the diseased liver to effect complete oxidation, or whether it is a manifestation of an acid intoxication or some other condition. Moreover, we are absolutely ignorant concerning the nature of the toxic material concerned, and whether it is derived from the fœtus or mother.

SYMPTOMS.

It is difficult to give a satisfactory definition of the pernicious vomiting of pregnancy, for the reason that the gradations between the ordinary morning sickness and the more severe forms of vomiting are often so gradual as to render it difficult to predict in a given case whether the condition may continue without injury to the health of the patient, or will pass into pernicious vomiting. Generally speaking it may be said that vomiting should be regarded as pernicious in character when it occurs so frequently as to interfere seriously with taking food, or leads to marked emaciation.

We are indebted to Dubois for the classical clinical picture of pernicious vomiting, which he divided into three stages. In the first the constant vomiting is associated with considerable emaciation and frequently with a troublesome dribbling of saliva. At the same time the urine becomes scanty and highly colored and the pulse somewhat accelerated. In

the second stage the vomiting becomes still more severe, the emaciation more pronounced and the breath assumes a peculiar acid and fœtid odor. As the patient becomes worse, the pulse increases in frequency and eventually there may be a slight rise in temperature. Finally in the third stage there is an apparent amelioration in the symptoms for a short time, during which the vomiting sometimes ceases and the patient and her friends become encouraged as to the outcome. Unfortunately, this is merely a transient condition, and the patient soon passes into a delirious or torpid condition and dies in coma or convulsions. During the last period there is no hope for recovery, which was not out of the question in the preceding stages.

My own experience has led me to believe that the clinical picture drawn by Dubois cannot always be followed at the bedside, as pernicious vomiting may occur either in an acute or chronic form, the latter being more frequent.

In the acute type, which according to my experience is always toxæmic in character, death may occur within ten days or two weeks after the onset of vomiting. In such cases the patient, who was previously perfectly well, or simply suffering from what appeared to be ordinary "morning sickness," suddenly begins to vomit everything she ingests, and soon presents signs of considerable prostration. The condition is usually associated with but little elevation in the pulse rate and fever is absent. After it has persisted for a number of days the patient begins to eject at frequent intervals and apparently with but little effort considerable quantities of dark, brownish, coffee-ground like material, and soon passes into a torpid condition and later dies in coma, which is sometimes disturbed by convulsions. (Cases 1 and 4.) This variety of vomiting is not necessarily associated with great emaciation, as one of my patients (Case No. 4) died while apparently well nourished and with a pulse of 96.

In the early stages of this form of vomiting the ordinary tests show that the urine is apparently perfectly normal, though naturally it is diminished in quantity on account of the small intake of fluids. In the last stages of the disease, however, it contains albumin, blood, and various varieties of tube casts, though this may be noted only a few hours before death. As a rule the temperature is not materially elevated; but occasionally shortly before death, it may reach a considerable height, and in one of my cases, not reported in this article, it registered 108° immediately before the fatal outcome. Occasionally in the last stages of the disease the patient may present an icteric discoloration of the conjunctivæ or even a decided icterus, though the latter is exceptional.

In the chronic form on the other hand, which may be toxæmic or neurotic in origin, the vomiting may continue for weeks or months, during which the patient becomes more and more emaciated, apparently entirely as the result of the ingestion of insufficient amounts of food. Under such circumstances she gradually becomes too weak to pursue her ordinary avocations and eventually is forced to take to bed. At the same time the pulse slowly increases in frequency, fever is usually absent and the black vomit of the acute variety is lacking until the very last stages of the disease. Consciousness is preserved until shortly before death, which is to be attributed in great part to inanition; while in the acute cases it is manifestly the result of an intoxication.

That inanition is the usual cause of death in the chronic variety has been generally recognized from the time of Dubois, and its importance was particularly insisted upon by Sutugin. Moreover, it is interesting to note that Frank in 1893, from the first study of the metabolism in this condition reached a similar conclusion, as he found that the quantity of nitrogen excreted by the urine was far greater than that taken in by the mouth.

In none of the cases which I have observed have the patients complained of disturbances in the olfactory sense, the so-called hyperosmia upon which Horwitz laid so much stress; though his observations in this regard are both interesting and significant.

The outline of the clinical history which I have just given applies particularly to cases of pernicious vomiting occurring in the first half of pregnancy. On the other hand, when it continues into the second half of pregnancy or originates in that period, the recognition of the significance of the condition becomes more difficult and the symptoms are frequently attributed to the typical pre-eclamptic toxæmia. Moreover, when the affection is associated with jaundice it usually presents the typical clinical picture of acute yellow atrophy; while if icterus is absent and the patient is only seen after she has passed into a comatose condition, it is quite natural to mistake the condition for eclampsia, especially as examination of the urine would show the presence of albumin, casts, and frequently blood.

Diagnosis.

Hyperemesis, as indicated above, should be diagnosticated whenever the vomiting becomes so constant that the patient is unable to retain any considerable quantity of food, or presents considerable emaciation. Much more important, however, than the mere diagnosis of pernicious vomiting, is the determination as to whether one has to deal with its reflex, neurotic or toxæmic variety, since upon this point depends the treatment to be pursued.

Accordingly, whenever a woman suffers from serious vomiting, even though it may not be absolutely pernicious in type, a careful vaginal examination should be made for the purpose of detecting any abnormality of the generative tract or ovum. The existence of a displaced uterus, an ovarian cyst, or a pelvic inflammatory mass is readily detected by the usual methods; while an increase in the size of the uterus out of proportion to the supposed duration of the pregnancy should arouse suspicion as to the existence of a hydatidiform mole or hydramnios.

On the other hand, it is extremely difficult to diagnosticate decidual endometritis with certainty, although its existence should be suspected when it is known that the patient suffered

from endometritis before conception, or when a dark brownish or brick-dust-colored discharge flows from the cervix. In the latter event, the occurrence of a spontaneous abortion may be expected.

If no abnormalities can be detected on the part of the generative tract or ovum, the diagnosis must lie between the neurotic or toxæmic types of vomiting. Unfortunately, as far as my experience goes, they cannot be differentiated positively by clinical symptoms, except at the terminal period of the affection, when it is too late to institute effective treatment, and therefore, our only resource lies in a thorough chemical examination of the urine, and the determination of the ammonia coefficient.

In order to make such a determination the entire amount of urine passed during the 24 hours should be collected, care being taken to place enough chloroform in the vessel to prevent decomposition. Then the total nitrogen should be determined by the Kjeldahl method and the amounts of urea and ammonia by the methods of Schoendorf and Schloessing respectively. In normal pregnancy, and even in neurotic vomiting, the ammonia coefficient varies from 3 to 5 per cent (Cases 5 to 7); while in the toxæmic type it may attain immense proportions, reaching 32, 38½, and 46 per cent respectively, as in cases 2, 3, and 4.

Thus far my experience with the toxæmic type of vomiting has not been sufficiently extensive to permit me to lay down definite rules as to the extent to which the ammonia coefficient may rise without particular danger to the patient; but at present it would seem that its increase to 10 or 15 per cent would justify the diagnosis of toxæmic vomiting, and would afford an urgent indication for the prompt termination of the pregnancy. In case 4 the ammonia coefficient was only 16 per cent when I first saw the patient, who did not appear to be seriously ill; and while it enabled me to make a diagnosis of the toxæmic origin of the vomiting, I felt justified in delaying interference and testing the efficacy of medicinal treatment. The outcome of the case, however, showed that I was in error, as the patient died in coma 48 hours after the induction of abortion with an ammonia coefficient of 46 per cent.

In addition to the determination of the total nitrogen and the urea and ammonia coefficients, it is if possible advisable to determine the other nitrogen subdivisions, as they may possibly throw still further light upon the nature of the condition. The urine should be likewise examined for the presence of leucin and tyrosin, which were absent in my cases, but were present in several of those examined by Ewing.

Unfortunately the determination of the ammonia coefficient cannot be undertaken by the ordinary physician in his office, but demands the services of a well trained chemist. In this connection it is extremely important to note that a rough estimate of the amount of ammonia cannot be made by determining the amount of urea by the Doremus apparatus, and assuming that a decrease in its amount indicates an increased ammonia coefficient, for the reason that with this test the ammonia as well as the urea is decomposed by the sodium hypo-bromite. Accordingly it might readily happen that the test would indicate the presence of a normal amount of urea, when in reality it was markedly diminished and its place taken by ammonia. This fallacy was exemplified in case 1, in which a normal urea output, as determined by the Doremus method, and the absence of albumin and casts caused me to overlook the toxæmic nature of the condition until death was imminent. I have already mentioned that a similar observation was made by Pierrehughes.

Another complication is that the determination of ammonia by the Schloessing method requires the best part of 48 hours, so that the result cannot be known for two days after the urine has been placed in the hands of the chemist. It is therefore to be hoped that the method of distilling the ammonia in vacuo will prove thoroughly satisfactory, as under such circumstances the determination can be made within a few hours. At present, however, this is a matter for decision on the part of the professional chemist and need not detain us here.

In connection with the question of diagnosis it is important to direct attention to the condition of the pulse, as it is generally stated that some idea of the severity of the case can be obtained from its character and frequency. My experience, however, has led me to believe that this is not necessarily true, since in case 4 the patient died with a pulse of 96. Moreover, a rise in temperature is not nearly so common as was believed by the early observers, and many patients die without any manifestation of fever. The occurrence of the black vomit on the other hand, is a sign of the greatest value and indicates a most serious condition; and although it cannot be said that its occurrence is necessarily indicative of death, it must nevertheless be regarded as of most ominous prognostic import.

In view of what has been said concerning the connection between acute yellow atrophy of the liver and the toxæmic type of vomiting, the occurrence of jaundice in pregnant women suffering from hyperemesis should always be regarded as ominous, and as indicating some serious derangement of the liver, rather than as a manifestation of a simple catarrhal condition.

When discussing the symptoms of the vomiting of pregnancy, particularly in the latter months, it was pointed out how readily it might be mistaken for eclampsia, especially if the patient were comatose; and Ewing has gone a step further and stated that he considers both acute yellow atrophy of the liver and eclampsia as manifestations of one and the same toxæmia. This conclusion, however, is so absolutely opposed to my own experience, which has taught me that the two diseases differ radically, whether considered from a clinical, chemical, or histological point of view, that I cannot allow it to pass unchallenged.

Clinically, eclampsia is nearly always preceded by a characteristic pre-eclamptic toxæmia, which is usually associated with pronounced general symptoms and early evidence of serious disturbance in the renal and circulatory functions—scanty urine, containing albumin and casts, and œdema. In

vomiting on the other hand, the urine is practically normal in amount until shortly before death, or at least is in direct proportion to the quantity of fluid ingested; whereas in the pre-eclampsia toxæmia it is always considerably diminished, notwithstanding the administration of diuretics and of large quantities of fluid by the mouth or rectum. Moreover, in vomiting, albumin and casts usually appear only in the terminal stage of the disease; while œdema is never present.

From a chemical point of view the difference is even more striking. In eclampsia there is usually a marked decrease in the total amount of nitrogen excreted, and while there may be a considerable diminution in the urea coefficient, pronounced variations do not occur in the ammonia coefficient, though occasionally it may rise to a slight extent. In vomiting, on the other hand, the total amount of nitrogen may be quite normal, while the amomnia coefficient becomes unusually high. (Compare charts 1 to 3 with 4 to 6.) My own experience would seem to indicate that an increase in the ammonia coefficient is of favorable prognostic import in eclampsia; whereas its significance is just the reverse in the vomiting of pregnancy.

From a pathological point of view, the lesions in the two conditions differ so markedly that I do not see how it is possible for anyone, who has once observed them, to consider that they are at all related. In eclampsia, as was first pointed out by Jürgens, Schmorl, and others, the lesion consists in hæmorrhagic necroses occurring in the portal spaces, dependent upon thrombotic processes in the smaller portal branches. At first they are sharply limited to the portal spaces, but as they enlarge, they invade the lobules from the periphery toward the centre; and are so characteristic that their mere presence justifies the diagnosis of eclampsia without any knowledge of the clinical history of the case. On the other hand, in the liver lesions accompanying the toxæmic vomiting of pregnancy the changes are purely degenerative in character, and begin about the central vein of the lobule and gradually extend towards its periphery. These differences are so sharply marked that it seems incredible to me that they could be confounded with one another.

After reading Ewing's article, I wrote to Schmorl, who has had the most extensive experience in the study of the liver lesions of eclampsia, and inquired whether he had ever seen the eclamptic lesions beginning in the center of the lobules. He replied in the negative and stated that they always began in the tissue about the periphery and only invaded the lobule itself secondarily. Moreover, Opie in his article upon zonal necroses of the liver, which was based upon material studied in the Pathological Laboratory of the Johns Hopkins University, stated that the lesions in eclampsia were highly characteristic, as it was only in that disease that they began at the periphery of the lobule, while in acute yellow atrophy the central or mid-zonal areas were the first to become involved. Therefore, from my own experience, as well as that of Schmorl, I cannot understand how it is possible for one to confound the lesions in the two conditions. Moreover, when one takes into consideration the difference in the clinical history and metabolism of the two diseases, the case becomes absolutely convincing.

From the evidence at present available, it would accordingly appear that we have to deal with at least two varieties of toxæmia of pregnancy, one giving rise to eclampsia or the pre-eclamptic toxæmia and the other to the vomiting of pregnancy and acute yellow atrophy, though it is quite within the range of possibility that further research will demonstrate the existence of still other varieties.

Prognosis.

Generally speaking it may be said that the prognosis is excellent in the reflex and neurotic forms of vomiting, provided they are properly treated. At the same time it must be admitted that patients suffering from them may succumb to inanition if proper measures are not instituted in good time.

In toxæmic vomiting, on the other hand, in view of the serious organic lesions and changes in metabolism, the prognosis is most grave and it seems safe to say that death will be the universal outcome if the toxæmia is pronounced, unless the pregnancy is promptly interrupted. Thus far, six examples of the toxæmic type have come under my observation (Cases 1, 2, 3, and 4 and two others not mentioned in this article), in all of which I felt obliged to induce abortion, but notwithstanding it, death occurred in 4 instances, a mortality of 66⅔ per cent. Of course these figures are not sufficiently large to justify one in drawing very general conclusions, but at the same time they clearly demonstrate the great gravity of the condition.

Treatment.

The treatment to be pursued in a given case of vomiting of pregnancy depends entirely upon the variety with which one has to deal. It is assumed that medicinal treatment has been tried without avail before the medical adviser comes to regard the case as at all serious.

If any abnormality of the generative tract or ovum be found it should be remedied as far as possible; the retro-displaced uterus should be replaced and held in position by a properly fitting pessary; ovarian tumors should be removed and inflammatory masses treated by appropriate anti-phlogistic measures. On the other hand, if hydramnios or hydatidiform mole be diagnosticated the pregnancy should be promptly terminated.

If the toxæmic variety of vomiting be diagnosticated, abortion should be induced as soon as its nature is fully recognized, as it would seem to offer the only chance of saving the patient, since the lesions associated with it are apparently incompatible with life if far advanced, and especially as there is no reason to suppose that they can be materially influenced by medicinal or dietetic treatment. After the uterus has been emptied, the patient should be given abundant saline injections by the rectum or subcutaneously if the former are not well borne. The stomach should be washed out occasionaly with a weak solution of sodium bicarbonate if the vomiting persists. No attempt should be made to feed the patient by mouth, and even

ice should be withheld until the vomiting ceases, all reliance being placed upon the salt infusion and enemata and the employment of rectal feeding.

On the other hand, if the neurotic variety of vomiting is diagnosticated, the treatment will depend to a considerable extent upon the impressionability of the patient. In certain exceptional cases a vigorous moral lecture may prove all that is necessary. In other instances the patient should be assured that her condition will not terminate fatally nor require the induction of abortion, and that it will probably yield to intelligent treatment. She should then be given some harmless remedy and receive the most minute directions as to the character of her food and the manner in which it should be taken. If such mild methods do not suffice, the patient should be put to bed in charge of a sensible nurse and the family and friends excluded from the room; all feeding by the mouth should be stopped and its place taken by the administration of saline and nutritive enemata by the rectum. Occasionally it may be necessary to add small quantities of laudanum to the enemata, or to give an occasional hypodermic of morphia.

If, however, such treatment is not followed by improvement within three or four days the patient should be threatened with removal to a hospital, and if the threat does not prove effectual, it should be carried out actually and the patient placed in a private room in a well regulated hospital, where a rigorous rest cure can be instituted upon the most approved plan. In my experience such drastic measures are rarely necessary, as the modified rest cure, as outlined above, will usually be followed by the cessation of vomiting within a few days and the vast majority of patients will be on the high-road to recovery within a week. (See Cases 5, 6, and 7).

Of course it is possible that occasional cases may not be amenable to such treatment and under such circumstances it may become necessary to resort to the induction of abortion in order to prevent death from starvation; though I believe that with an accurate diagnosis and sufficient assurance on the part of the physician, such a resort will become less and less frequently necessary, and that the operation will be reserved almost entirely for the cases of toxæmic vomiting.

HISTORY OF CASES.

CASE I.—*Toxæmic vomiting. Mrs. P.* (Fig. 1.)

I first saw the patient on April 22, 1903, when she desired to ascertain whether she was pregnant. She was a tall, thin, delicate-looking woman, 28 years old, who had been married two years and had never been pregnant. Her last menstrual period occurred on February 10 and lasted five days, but in March and April there was a slight flow at the regular time, but much less abundant than usual. Prior to seeing me she had suffered a good deal from nausea.

On examination the uterus was found to be enlarged to the size of a two-months' pregnancy and softened, so that there was little doubt about the diagnosis.

A few days later I saw the patient again, when she was complaining intensely of nausea and vomiting, for which I regulated the bowels and ordered some capsules of pepsin and nitrate of silver. As these were without effect, various other remedies were employed with the same result. Gradually the nausea and vomiting became so intense that the patient was unable to retain anything at all, so that on May 6 I resorted to rectal feeding and ceased all attempts to administer food by the mouth. From this time she received two nutritive enemata daily consisting of 12 oz. of peptonized milk and 2 eggs, as well as a third enema of 750 cc. of salt solution. The enemata were borne extremely well and gave no discomfort, but nevertheless the patient grew weaker and more emaciated and still suffered severely from vomiting. Her pulse, which was 70 when I first saw her, slowly rose to 92.

On May 15 I asked her physician, Dr. W. F. Lockwood, to see her in consultation. At that time she was suffering intensely from profuse salivation and was constantly vomiting small quantities of a dark brownish-looking fluid and complaining of intense pain in the epigastric region. In spite of the comparatively low pulse, it was decided that the prompt induction of abortion was indicated, which was done on the afternoon of the 16th.

The cervix was dilated without great difficulty by means of Goodell's and Hegar's dilators sufficiently to permit the introduction of one finger into the uterus. The ovum was then detached from the uterine wall and broken up into small pieces, which were readily removed by means of ovum forceps. A douche of sterile salt solution was then given. During the attempt to introduce the finger into the uterus the outlet was considerably torn, so that it was necessary to repair it with three silk-worm gut sutures.

The patient stood the operation well and was put back to bed in good condition. For the following 18 hours her condition improved markedly, and the nausea and vomiting ceased entirely. At the end of that period they reappeared, however, and the patient constantly vomited small amounts of a coffee-ground-like material with almost no effort. This could only be checked by the administration of morphia hypodermically, which was continued throughout the 17th and 18th, but before its administration her condition became torpid and she gave the impression of suffering from a profound toxæmia.

Gradually the pulse became quicker and in spite of the administration of nutritive enemata, subcutaneous salt infusions, and the hypodermic use of digitalis and strychnia, it became more and more rapid. On the morning of the 19th it reached 119, and slowly increased in frequency until she died at 9 p. m. The temperature was perfectly normal until the morning of the day of death, when it reached 101.5°. During the last 12 hours of life the patient was absolutely unconscious and died without an effort.

The urine was examined several times during the illness and the day before the induction of abortion the 24-hour specimen amounted to 750 cc. and contained 30 grammes of urea as estimated by the Doremus ureometer. There was no trace of albumin, while microscopic examination was negative. No examination was made after the operation, so that it cannot be said whether albumin was present or not, though from the condition of the kidneys at autopsy, its absence would have been surprising. Unfortunately an accurate chemical examination of the urine was not made in this instance.

ABSTRACT OF AUTOPSY PROTOCOL. No. 2110. DR. H. T. MARSHALL.

Anatomical Diagnosis.—"Recent laceration of the vagina with infiltration into adjacent tissues. Lacerated cervix. Portion of placenta adherent to and growing into uterine wall. Uterus of early pregnancy. Fatty degeneration, areas of necrosis and bile staining of liver. Fatty degeneration and bile staining of kidneys. Chronic adhesive pleurisy left side. Old latent tuberculosis of two-thirds of upper lobe of left lung. Scar at right apex."

Body of a well-built, sparely nourished woman. No œdema.

No jaundice. Pupils equal. Slight post-mortem discoloration of dependent parts. Subcutaneous fat slight in amount.

Peritoneal cavity negative.

Thorax.—Pleural cavities dry. Right pleural cavity is clear. On the left side dense adhesions between upper lobe and chest wall. Pericardial cavity clear.

Heart.—Apparently normal: valves clear. Myocardium is soft, opaque, yellowish, and apparently bile stained.

Lungs.—Upper lobe of left lung greatly reduced in size. Contains a few calcified and caseous foci. Small apical scar in right lung.

Fig. 1.—Showing Central Necrosis of Liver Lobule.

Liver.—Weight 1000 grammes. Is small and of a bright yellow color, with smooth surface and soft consistence. On section it presents a very fatty, bile-stained appearance, with areas of degeneration and necrosis evident to the naked eye. The capillaries stand out very prominently between the fatty and yellow strands. Except that the degeneration is not so extreme, the section suggests acute yellow atrophy. No nodules in liver. Gall-bladder normal.

Stomach.—Is small and contains about 500 cc. of dark fluid, containing blood cells, bile, and débris. Mucosa normal.

Intestines, spleen, pancreas, and *thyroid* normal.

Kidneys.—Both kidneys present an identical appearance and are considerably enlarged. The capsule strips off readily leaving a bile-stained, opaque, yellow surface, with no vessels showing. On section the cortex measures 7 to 8 mm., is very yellow, opaque, and granular and slightly raised above the level of the pyramids. No structures, vessels, or glomeruli can be made out. The pyramids are pale and their periphery shows lines and areas of fatty appearance, which is particularly marked in their outer third. The renal pelves are normal.

Genitalia.—Bladder normal. Tubes and ovaries normal. Uterus appears normal, and measures 11 cm. from fundus to cervix and 8 cm. between the insertions of the tubes. The external os is roughened and shows some superficial necrosis. On section the uterine cavity appears clear and normal, except a rough, shaggy, reddish area, which projects 6 to 7 mm. above the general surface on the posterior wall, near the fundus and extending to the right cornu. On section this presents a soft and somewhat friable appearance and extends some distance down into the muscular wall. It appears to be decidedly infiltrating, but no signs of it can be found outside of its original boundaries.

Microscopic Examination. Liver.—Under the low power, sections of the liver stained with hæmatoxylin and eosin present a remarkably mottled appearance, about one-half of the section being occupied by rounded and irregularly shaped areas which stain bright pink with eosin and are separated from one another by less brightly staining tissue. Upon closer examination it is seen that these areas correspond to the central portions of the liver lobules, all of which are involved in the process. The individual lobules are sharply marked off from one another and the interlobular spaces present a normal appearance with connective tissue, blood-vessels, and bile-ducts. Nowhere is there any hæmorrhage into the portal spaces, nor any trace of thrombosis of their vessels.

In each lobule three distinct zones may be distinguished: peripheral, midzonal, and central. The peripheral zone consists of one or two layers of practically normal liver cells with brightly staining nuclei and a faintly granular protoplasm. In places even this narrow zone of normal cells is imperfect, so that the cells of the midzonal layers of adjacent lobules abut directly upon one another. The midzonal portion of the lobules varies in thickness, but in general occupies one-half of the distance between the central vein and the periphery. It is made up of large, irregularly shaped cells, whose nuclei stain fairly well and whose protoplasm is almost entirely replaced by a number of vacuole-like structures nearly as large as the nuclei. These probably represent the location of fat droplets, which were dissolved out by the hardening fluids, but as osmic acid specimens were not available, positive statements cannot be made in this regard. In this layer, there is considerable engorgement of the intralobular capillaries. The connective-tissue elements are well preserved and in places appear somewhat increased in number. No leucocytes are present. The central portion of each lobule, which occupies at least half of its total area, is marked off from the midzonal layers by an irregular, wavy line, though in places it is perfectly apparent that the two portions merge into one another. The central portion stains brightly with eosin, and in many lobules is made up of absolutely necrotic cells with a coarsely granular structure, no nuclei of any kind being visible. In others an occasional connective-tissue nucleus can be distinguished, while in rare instances the degenerated nuclei of some of the liver cells take on an indistinct stain with hæmotoxylin. In some of the lobules there is a well-preserved central vein; in others its location is indicated by a mass of nuclei, while in still others all trace of it has disappeared. (Fig. 1.)

Kidneys.—Sections show that the glomeruli present a practically normal appearance. The secretory portion of the renal tubules on the other hand is almost entirely necrotic and the cells of the tubules are converted into irregular, coarsely granular, vacuolated masses, which contain only an occasional faintly staining nucleus. In many places the lumina of the tubules are obliterated, while in others they are more or less completely filled with granular material, which occasionally contains red-blood cells. The collecting tubules, on the contrary, appear to be perfectly normal and their cells stain in the typical manner. The connective tissue portion of the kidneys appears unchanged.

Uterus.—Sections through the projection at the fundus, which was noted at autopsy, show that it is composed almost entirely of fibrin, but immediately adjoining the uterine wall it encloses a few chorionic villi, which present a normal appearance. The decidua presents its characteristic structure, except that it appears richer in fœtal cells than is usually the case.

Placenta.—Sections through the placenta removed at the time of operation present the appearance characteristic of early pregnancy. The villi are covered by two layers of epithelium—syncytium and Langhans' layer—and present a myxomatous stroma, which contains but a few blood-vessels. Many giant cells are present in the intervillous spaces and occasional trophoblastic islands are seen.

CASE II.—*Toxæmic Vomiting. Mrs. A. Chart No. 1.*

The patient was seen October 26, 1903, in consultation with Dr. James Bosley, from whom I obtained the following history: 29 years old, has been married 7 years, but has never been pregnant; has always been perfectly healthy, although of a somewhat nervous disposition. The last menstrual period occurred on August 1, 1903. On September 9 she began to suffer from nausea and vomiting, which gradually became worse in spite of vigorous treatment. For the past two weeks the patient has been unable to retain food and has vomited almost constantly. She has lost approximately 20 pounds in weight. The day before I saw her she had been seen in consultation by Dr. I. E. Atkinson, who recommended the induction of abortion.

Examination showed a very emaciated patient with eyes sunken far back in their orbits. She complained of intense pain in the epigastric region and stated that she vomited almost constantly. At the side of the bed was a basin containing a quantity of coffee-ground-like material which she had recently vomited. The patient looked extremely ill; her pulse was 132 and temperature normal. The heart and lungs were normal. There was apparently a slight

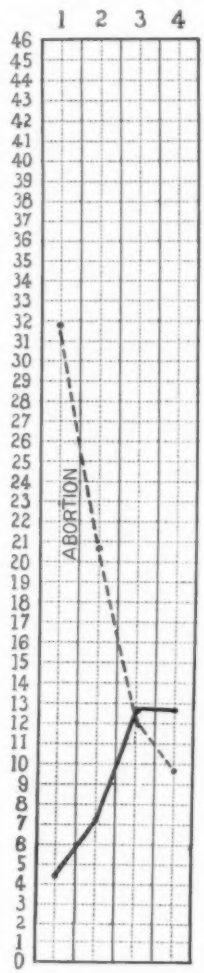

CHART 1.—Toxæmic Vomiting.

In this and the following charts, the solid line indicates total nitrogen and the broken line ammonia. Each square of the chart corresponds to 1 gramme of nitrogen and 1% of ammonia. The figures at top of charts indicate the day of observation.

diminution in the liver dullness, whose lower edge was two fingers' breadth above the costal margin. On palpation the fundus of the uterus could be felt just above the pubes.

In view of the serious condition of the patient it was determined that abortion should be brought on the following day. The delay was for the purpose of allowing the collection of a 24-hour specimen of urine. A trained nurse was procured and instructed to administer two rectal enemata of 500 cc. of salt solution during the next 24 hours. As soon as the first specimen of

urine, which amounted to 500 cc. had been collected, the operation was proceeded with.

Examination at that time showed the vagina was short and the external os small, hard, and virginal. The cervix was dilated by means of Goodell's and Hegar's dilators until the index finger could be readily introduced into the uterus, which required about 25 minutes. The ovum was then separated from its attachment by the finger, its fragments being removed by means of an ovum

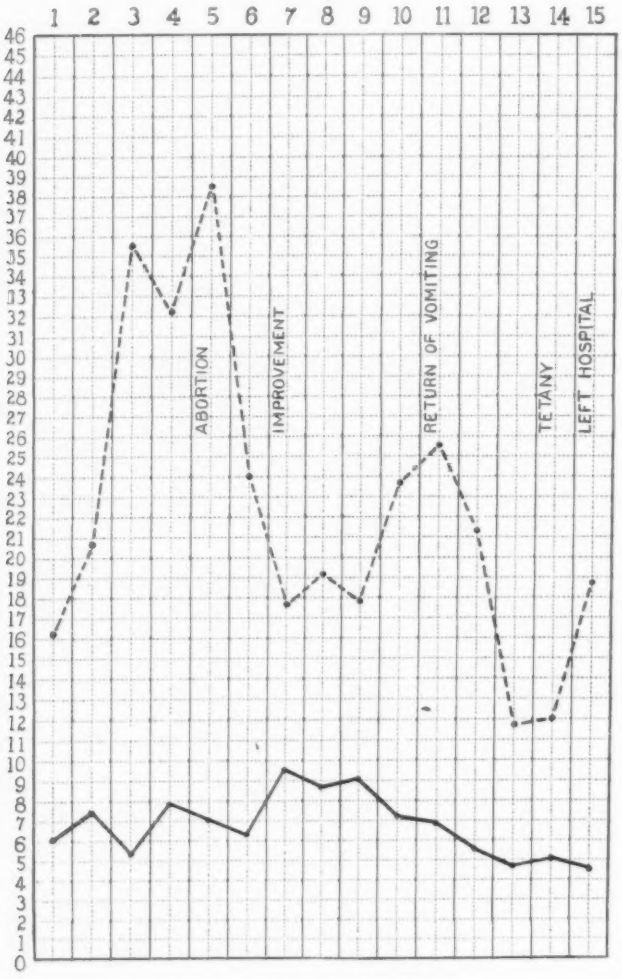

CHART 2.—Toxæmic Vomiting.

forceps. A uterine douche was then given and the uterus packed with gauze. The patient stood the operation well and was put back to bed in good condition with a pulse of 124.

She began to improve almost immediately after the operation, and within 24 hours the pulse had become slower, the nausea had practically ceased and a marked change in her general appearance was noted. After this convalescence was so rapid that it was unnecessary for me to see the patient after the 4th day. The pulse reached 72 on the 6th day after operation, and the highest temperature was 100.4° on the 2d day.

Chart No. 1 gives a graphic idea of the condition of the urine, which for the 24 hours immediately preceding the operation presented an ammonia coefficient of 32%. Albumin or casts were at no time present. The specimen of urine examined one month later was perfectly normal, with an ammonia coefficient of 4%.

CASE III.—*Toxæmic Vomiting. Mrs. C. Obst. No. 1710, J. H. H. Chart No. 2.*

The patient was seen on February 25, 1904, in consultation with Dr. Geo. B. Reynolds, when I obtained the following history: 37 years old, married 14 months. One miscarriage at 2 months 8 months ago. Was in excellent health prior to the present illness. The last menstrual period began December 13, 1903. Four weeks later the patient began to suffer with indigestion, which was soon followed by nausea and vomiting, accompanied by violent pain in the epigastric region. For the past three weeks the nausea and vomiting has been intense, no solid food being retained for the past two weeks, and for the past two days even the blandest fluids cause immediate vomiting. During this period she has suffered almost constantly from severe headache, and has lost 15 to 20 pounds in weight.

On examination the patient was found to be a small, emaciated woman with a pale and haggard face. The lips and mucous membranes were without color and the tongue thickly coated. She was vomiting small quantities of clear fluid at frequent intervals. Auscultation revealed no abnormalities; pulse 120 and weak, temperature normal. The liver dullness was normal. The abdomen was not distended or painful on pressure. The fundus of the uterus could not be felt above the symphysis pubis. Vaginal examination negative, except for 8 to 10 weeks' pregnant uterus.

On account of her surroundings the patient was immediately transferred to the Johns Hopkins Hospital, where she was kept under observation for four days and nourished almost exclusively by the rectum and given copious enemata of saline solution. During this period the fluid intake and output were carefully measured and the amount of total nitrogen and the ammonia coefficient determined. At the end of this time her condition was worse rather than better, and as seen from the accompanying chart, the ammonia coefficient reached 35.5% on the 3d day.

In view of her condition it was thought best to attempt the induction of abortion by a bougie, which was readily introduced without anæsthesia at noon February 29, when her temperature was 99.2° and pulse 112. As the bougie did not bring on uterine contractions, it was removed the following morning and the uterus emptied by means of the finger and ovum forceps. The patient stood the operation well and was put back to bed in good condition.

Following the operation the patient improved slowly until March 5, when she became torpid and drowsy and gave the impression of being profoundly intoxicated. At the same time the nausea and vomiting, which had almost ceased, increased in severity. As seen by the chart this was accompanied by a rise in the ammonia coefficient from 18 to 25%. Following this there was improvement for several days until the 9th of March, when the nausea and vomiting reappeared and the patient developed a tetany, which continued for two days. During this period the nausea and vomiting were very severe and the patient impressed one as being desperately ill, the pulse varied between 88 and 100 and was of poor volume. By March 11 her condition had improved considerably and the nausea had disappeared, so that she was able to take two meals of solid food during the day. As the patient had become dissatisfied with the hospital, she was allowed to go home at this time, although far from well.

She eventually made a good recovery and on returning to the hospital the following May had so improved in appearance that she was not recognized. The urinary examination at that time showed an ammonia coefficient of 4%.

At no time during the illness were albumin or casts present in the urine. The highest temperature was 100° F. on the day of

abortion. Chart No. 2 gives a good idea of the relation between the total nitrogen and the ammonia coefficient.

CASE IV.—*Toxæmic Vomiting. Mrs. S. Obst. No. 2116. Chart No. 3.*

The patient was seen on March 20, 1905, in consultation with Dr. A. K. Bond, from whom I obtained the following history: 33 years of age, married October, 1904, no previous pregnancies. No serious illness, except typhoid fever five years ago. He was first consulted on the 13th of March, when the patient stated that she believed that she was two months pregnant, having menstruated last January 13, 1905. The next day she complained considerably of nausea and vomiting, which had begun February 20, 1905, and asked that something be done to relieve it. Simple remedies were administered without effect. By March 17, the vomiting had become so distressing that nothing could be retained by the stomach. The vomited matter consisted either of recently ingested food or of a clear, colorless, odorless and tasteless fluid. The only thing that seemed to give relief was morphia administered hypodermically. The bowels were constipated and resisted the strongest purgatives.

The patient is a large, well-nourished woman with a bright complexion and anxious expression, who is lying in bed and making almost constant efforts to vomit, but expelling only small quantities of clear fluid.

On examination the heart and lungs presented no abnormality; the pulse was 68 and of good volume. The liver dullness was apparently normal. No tenderness of abdomen on palpation. No jaundice. Vaginal examination showed a nulliparous outlet, the cervix virginal and quite hard; the uterus in normal position, soft in consistency, and enlarged to the size of an 8 to 10 weeks' pregnancy. Appendages normal.

I advised the stoppage of all attempts at feeding by the mouth and the daily administration of four high saline enemata of 400 cc. each. A trained nurse was obtained, who was directed to save a 24-hour specimen of urine. The first specimen measured a little over 500 cc. and contained 7.5% grammes of total nitrogen with an ammonia coefficient of 15.8%. Microscopic examination was negative except for the presence of amorphous urates.

A diagnosis of toxæmic vomiting was made on the strength of the high ammonia coefficient, but in view of the apparently satisfactory general condition of the patient, it was thought that immediate interference was not indicated.

Her condition continued the same on the 22d, but unfortunately the urine was not saved. On the 23d the vomiting became more intense and the matter vomited changed from a clear mucus to a dark greenish or brownish fluid material. The ammonia coefficient was 15.3%. When I saw the patient on the morning of the 24th, I recommended her removal to the hospital for the immediate termination of pregnancy, in view of the change in the appearance of the vomit and the continued high ammonia coefficient. Urine drawn by catheter just before the operation presented an ammonia coefficient of 21.3%.

The patient was anæsthetized by chloroform, and, after the usual preparations, the cervix was dilated with Wathen's instrument, followed by Hegar's bougies. It was so resistent, however, that only a No. 17 bougie could be introduced, after which the uterus was cleaned out by a dull curette and ovum forceps, followed by a hot intra-uterine saline douche and a pack of iodoform gauze. The patient stood the operation well and was put back to bed in good condition.

During the night following the operation the patient improved considerably, vomited but little and was very comfortable. When I saw her at 2 p. m. on the 25th she was looking better than before the operation, was in excellent spirits, and stated that she had not vomited since 10 o'clock the previous evening.

During the afternoon she became more uncomfortable and suffered so extremely from nausea that her stomach was washed out with a weak solution of sodium bicarbonate at 6.45 p. m. and a considerable amount of dark brown material removed, after which considerable relief was obtained. The patient passed a restless night, in spite of the administration of two hypodermics of ⅛ gr. of morphia. She became very restless about 3 a. m. March 26, when her stomach was again washed out and a large amount of apparently blood-stained material siphoned off.

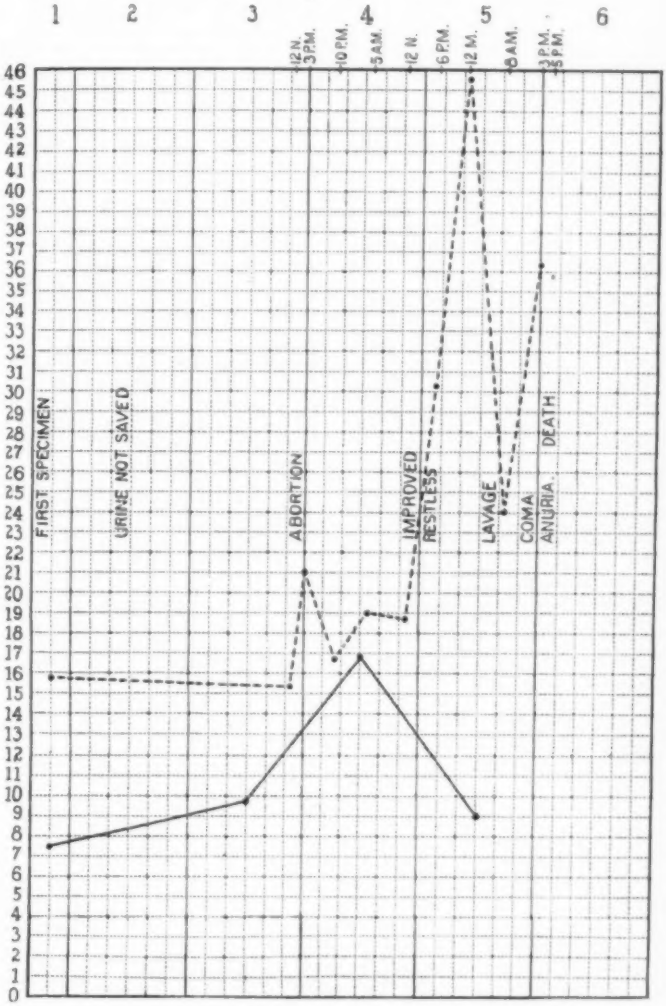

CHART 3.—Toxæmic Vomiting.

When I saw her at 11 a. m. her condition had changed markedly as compared with the previous day. She was very torpid and the pupils were quite tightly contracted, which it was thought was possibly due to the morphia. The pulse was more rapid than the day before and of poor volume, but did not exceed 100. The liver dullness was unchanged and there was no great tenderness over the lower abdomen. At this time a slight yellowish coloration of the conjunctivæ was noted. The stomach was again washed out and the material removed contained large quantities of brownish, reddish flakes, which under the microscope were found to be composed of blood cells. During the afternoon the patient became irrational and restless and tossed wildly in bed;

shortly afterwards she became comatose and remained so until she died at 6 p. m.

Prior to 3 p. m. as shown by the urinary chart, urine was excreted freely, but catheterization at that time yielded only 150 cc. of bloody urine, and at 5 p. m. only 4 cc. of apparently pure blood was obtained.

From the time I first saw the patient nothing was administered by the mouth, but large quantities of salt solution were given by

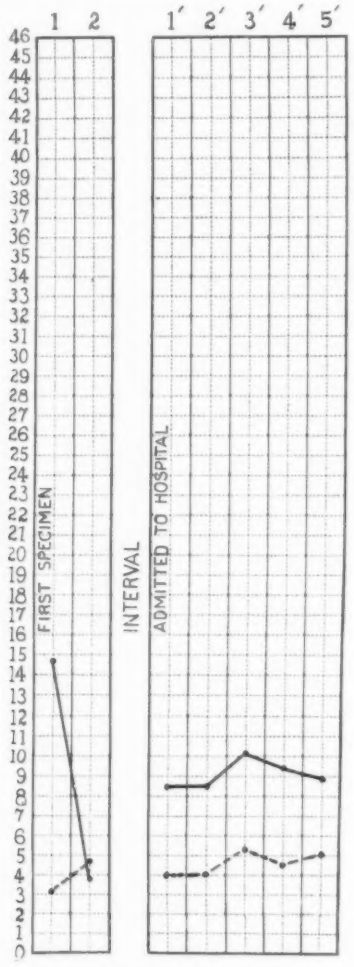

CHART 4.—Neurotic Vomiting.

the rectum, as well as occasional nutritive enemata after her admission to the hospital.

Before admission to the hospital the entire 24-hour specimens of urine were examined, but after the operation she was catheterized and the ammonia coefficient determined in each specimen, though the total nitrogen was estimated from the total 24 hours' output of urine.

From the accompanying chart (No. 3) it is seen that the ammonia coefficient remained between 15 and 16% for several days, but rose to 21.3% just prior to the induction of abortion, while the total nitrogen was practically normal. The high total nitrogen after the abortion was probably due, in part at least, to the involution of the uterus. As the patient became worse the ammonia coefficient rapidly rose and reached 45.5% 46 hours after the abortion. The sudden drop immediately after this was probably due to the lavage with sodium bicarbonate, as it had risen to 36.5% in the specimen obtained three hours before death.

It is interesting to note that albumin or casts were not present until the day of death, the first trace of albumin being noted at 8 a. m., together with a few hyaline and granular casts. Seven hours later albumin was present in large quantity and casts were extremely numerous; while the last catheterized specimen consisted of only 4 cc. of blood. Leucin and tyrosin were not present.

At no time during the illness did the patient show any signs of emaciation, and just before death presented the appearance of a well-nourished woman with a ruddy complexion.

The temperature at no time was elevated, its highest point being 99.2° F. The pulse remained persistently low, and shortly before death, after it could no longer be felt at the wrist, was found to be 98 on auscultation.

CASE V.—*Neurotic Vomiting. Mrs. C. Chart No. 4.*

I first saw the patient November 14, 1904, when I obtained the following history: 28 years old, married 9 years, two children and one miscarriage. The labors were difficult but not instrumental. General health excellent, except in last and present pregnancy. The last menstrual period occurred September 5, 1904. Almost immediately after missing the October period vomiting began, which after a couple of weeks became so frequent and intense that she was hardly able to retain food of any description, and as a consequence has lost considerably in weight. Heart, lungs, liver, and genitalia normal. Pulse 96, temperature normal.

As shown by Chart 4, two 24-hour specimens of the urine examined at this time presented a normal ammonia coefficient. Shortly afterwards a slight, bloody discharge appeared and the patient believed that abortion was imminent. As long as this continued, she did not vomit; but as soon as the hæmorrhage ceased, the vomiting reappeared with its original intensity, so that I was urged to induce abortion, as the various remedies which I prescribed were without avail.

In the latter part of November the patient had a number of severe asthmatic attacks, similar to those from which she suffered throughout the second half of her last pregnancy. On December 1 her condition became so serious that she was transferred to the hospital. When I saw her shortly after admission she was sitting propped up in bed and gasping for breath, with labored respiration and a marked respiratory tug, and with loud rales over both lungs. The pulse was 116 and the temperature normal. She was considerably emaciated, with her eyes sunken far back in their orbits, and gave the impression of being desperately ill.

From the examination of the urine and the history of the case I felt convinced that a large part at least of the symptoms were neurotic in origin, and accordingly placed her under the care of a competent trained nurse and ordered a diet of measured quantities of water, milk, and egg albumin, and the saving of all urine. She was told that her vomiting was not of such a character as to necessitate abortion and would undoubtedly yield to treatment. As a result the vomiting ceased within 48 hours, while the asthmatic attacks became less frequent and severe. Improvement was so rapid that at the end of five days she was able to retain a more liberal diet, and left the hospital on the 10th day greatly improved. The second part of Chart 4 shows the condition of the urine during the first five days of her stay in the hospital.

The vomiting did not reappear after her return home, but within a short time the asthma grew worse and gradually became so severe as to appear to menace her life. Accordingly after consultation with her physician, Dr. Cary B. Gamble, she was

once more removed to the hospital and abortion was induced on the 29th of December. With the exception of two days one week after the operation, the asthmatic attacks ceased with the administration of the chloroform. The convalescence was uneventful and the patient returned home in excellent condition.

CASE VI.—*Neurotic Vomiting. Mrs. McN. Chart No. 5.*

I first saw the patient February 12, 1905, when I obtained the following history: 25 years old, married 3 years, no children, one abortion at 2 months shortly after marriage. Last menstrual period December 21, 1904. She was perfectly well until February 1, 1905, when she began to suffer intensely from nausea and vomiting; for the past week she has vomited everything she has taken and has lost considerably in flesh and is extremely nervous.

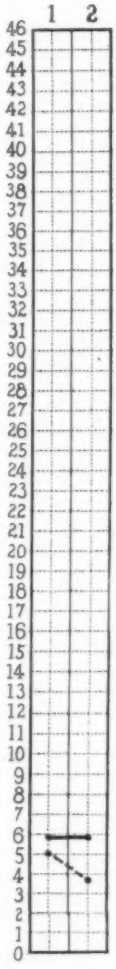

CHART 5.—Toxæmic Vomiting.

Physical examination showed no abnormalities and the genitalia were normal, except for the pregnancy. Pulse 100, temperature normal. In spite of the administration of a number of remedies, the vomiting grew worse rather than better. Accordingly a 24-hour specimen of urine was saved on the 18th and 19th and found to be normal, as shown in Chart 5.

Having diagnosticated neurotic vomiting from the normal condition of the urine, I told the patient that there would be absolutely no necessity for interfering with the pregnancy and that she would be promptly cured if she would implicitly follow my directions. I then put her to bed and gave very minute directions as to the character of her food and how it should be taken.

When I saw her again on the 27th her condition had not improved. I accordingly told her that there was no doubt about her ultimate recovery, but that if she did not cease vomiting within three days, I should take her to the hospital, put her under a trained nurse, not allow her to see her family, and institute a rigid rest cure. Upon calling three days later to learn

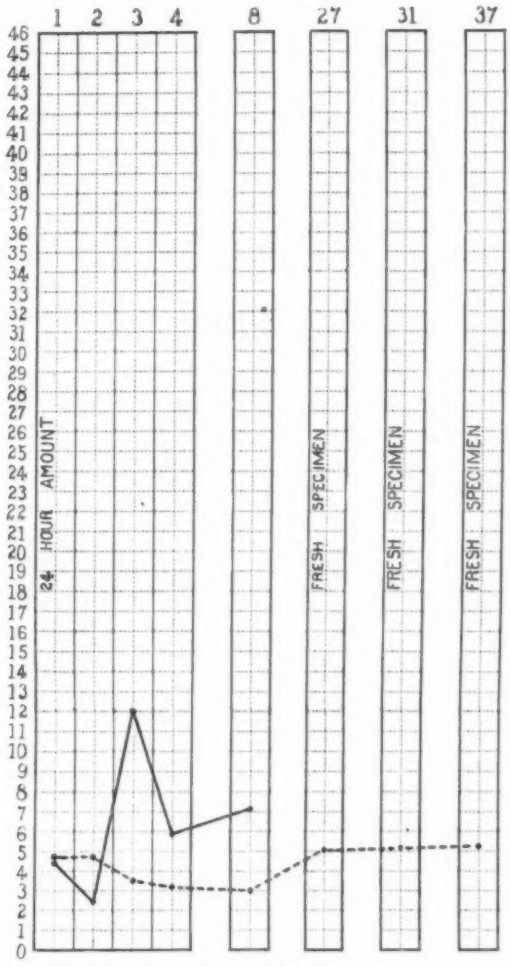

CHART 6.—Toxæmic Vomiting.

the effect of my threat, I found that the patient had not vomited since my last visit and had been able to eat three meals a day with great comfort ever since.

The vomiting did not recur and the patient improved markedly in appearance, so that one month later she was stouter than ever before in her life. She told me later that I could not have made a more fearful threat, as she had an abnormal horror of a hospital and would have done anything to escape going to one.

CASE VII.—*Neurotic Vomiting. Mrs. W. Chart No. 6.*

I first saw the patient April 12, 1905, in consultation with her husband, who is a physician. She was 21 years old, married 16 months, and had not been pregnant. The last menstrual period

occurred February 5, 1905. She began to suffer from nausea and vomiting just after missing her March period. At first the vomiting occurred at regular intervals, but for the past three weeks it has occurred after every meal, sometimes at once and at other times not for several hours. Several days ago she fainted while vomiting. A week before I saw her she had gone to the seashore, but was not benefited by the trip. She has lost considerably in weight and complains of pain in the epigastric region.

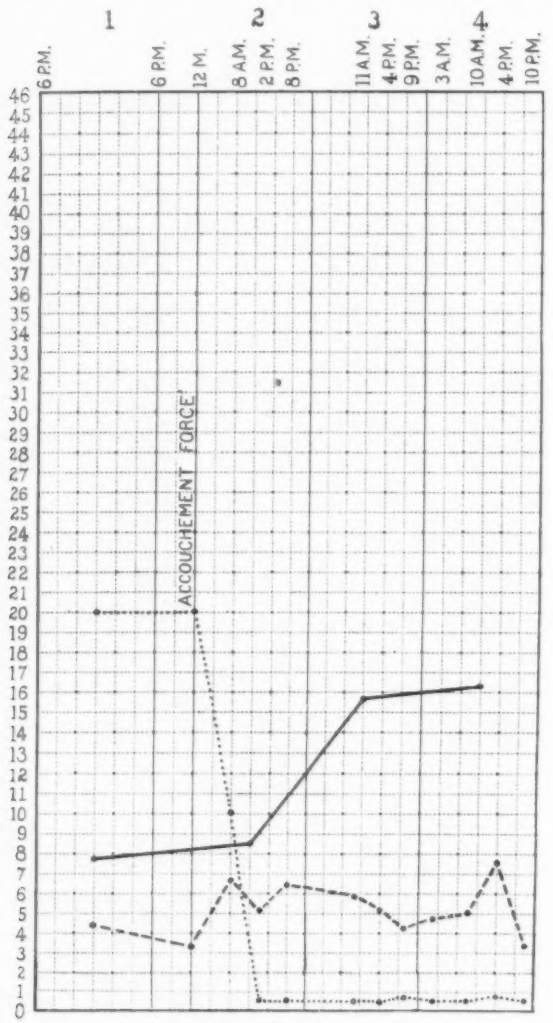

CHART 7.—Pre-eclamptic Toxæmia.

Dotted line represents albumen. Each square corresponds to one gramme per litre of urine.

She is very nervous and told me that her mother in all of her pregnancies had suffered with intense nausea, which on several occasions was so severe that the induction of abortion was considered.

Examination showed a small, thin woman, with no jaundice or œdema. The heart and lungs were normal; pulse 120, temperature normal. The abdomen was scaphoid and the liver dullness seemed slightly diminished, terminating 5 cm. above the costal margin in the mammary line. The genitalia were normal and the uterus enlarged to the size of a 7 to 8 weeks' pregnancy.

The patient was put to bed and a 24-hour specimen of urine collected, which, as shown by Chart 6, presented a normal ammonia coefficient. Accordingly a diagnosis of neurotic vomiting was made. The patient was assured that she would recover promptly if she followed my directions, and a trained nurse was obtained and ordered to allow no one in the room but the husband and then only for a few minutes a day. She received saline enemata each day, but no food for the first 24 hours, and only albumin and water afterwards. Within two days the vomiting ceased and two days later small amounts of food were given by the mouth, and by the end of the week the patient was able to go about in comfort.

Her condition remained very satisfactory for nearly three weeks, when the vomiting returned and soon became more severe than before. The patient rapidly emaciated, and her husband felt that the only hope for her recovery lay in the induction of abortion. A more rigorous trained nurse was secured, the patient put back to bed and nourished only by the rectum and told that she could not see her friends nor receive anything by the mouth until the vomiting ceased; and that if that did not occur within a few days she would be taken to the hospital and completely isolated. On this occasion recovery was slower, but within 48 hours the nausea had become less violent, and the vomiting ceased two days later, although the patient still complained of great depression and felt that her recovery was merely temporary. Shortly afterwards she was allowed small quantities of solid food and began to move about the room. After this improvement was rapid, and a few days later when I telephoned to inquire how she was, I found she was dressing to go to the Horse Show. She rapidly regained her loss in weight and has since been in excellent condition.

CASE VIII.—*Pre-eclamptic Toxæmia. Mrs. C. Chart No. 7.*

Typical clinical history. Induction of premature labor. Compare this Chart with Charts 1 to 3 in cases of toxæmic vomiting.

I am under many obligations to my associate, Dr. J. M. Slemons, for the chemical examination of the urine in the cases here reported.

CONCLUSIONS.

1. The pernicious vomiting of pregnancy is not due to a single etiological factor, and occurs as one of three varieties, reflex, neurotic, and toxæmic.

2. The reflex type is dependent upon the existence of abnormalities of the generative tract or ovum and may be cured by their correction or removal.

3. The neurotic type is dependent upon the existence of a neurosis without demonstrable lesions and is more or less allied to hysteria. It is the most frequent variety of serious vomiting and can be cured by suggestion or a modified rest cure.

4. The toxæmic type is associated with characteristic changes in metabolism and in fatal cases, at least, with lesions in the liver analogous to those observed in acute yellow atrophy. It may occur in an acute or chronic form, the former causing death in 10 days or less, while the latter may persist for weeks or even months.

5. In reflex and neurotic vomiting there are no manifest changes in the urine, while the toxæmic variety is characterized by a marked decrease in the amount of nitrogen excreted as urea and a characteristic increase in the amount excreted as ammonia. The so-called ammonia coefficient rising from 3 to 5 per cent to as high as 46 per cent in one of my cases.

6. The toxæmic type is diagnosticated by the examination of the urine, the reflex by careful bimanual examination of

the genitalia, and the neurotic after the exclusion of the other two varieties.

7. The prognosis is excellent in reflex and neurotic vomiting, provided appropriate treatment is instituted, so that the termination of pregnancy is rarely indicated. In toxæmic vomiting, on the other hand, a fatal issue can be averted only by the prompt induction of abortion, and even then the prognosis is dubious.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

December 18, 1905.

Dr. W. G. MacCallum in the chair.

Exhibition of Surgical Cases. MR. LANGNECKER, MR. HELMHOLZ, AND DR. CUSHING.

CASE I. RUPTURED BRACHIAL PLEXUS.—The patient presented by Mr. Langnecker came under Dr. Cushing's observation on October 10, with complete traumatic paralysis of his left arm. Examination showed great atrophy of the entire musculature of the arm and shoulder girdle. The muscles were flaccid and give the reaction of degeneration. The arm was anæsthetic to all forms of sensation over an area corresponding to the skin fields of the fifth cervical to the first thoracic segments inclusive. At no time following the injury had he suffered pain.

Operation.—On thoroughly exposing the plexus, which was found densely bound up in connective tissue, the fifth and sixth roots were disclosed; the root of the seventh was missing; the root which had the appearance of the eighth was very much arched, and beneath this was a stump giving the appearance of the ruptured seventh. This stump was refreshed and sutured into the plexus at the region of the junction of the fifth and sixth roots which, after being freed from scar tissue, were found to have their continuity intact. The wound was closed and the patient made an uneventful recovery. Before operation there had been no sensation in the arm except on its post-axial surface just above the elbow (second thoracic field), and in the axillary region where there was some hyperæsthesia. The pupil on the left side was more contracted than on the right; the tension of the left globe was lower than the right; and there was a narrowing of the palpebral cleft. The under part of the arm was mottled and cyanosed; the member hung flail-like and the forearm was rotated inward and pronated. The humerus was very loose at the articulation and seemed merely to hang in the capsule. Since operation the patient has received daily massage and galvanism. The ocular symptoms have changed greatly but there still remains a trace of the sympathetic paralysis. There has been no return of motion in the arm, though there is slight voluntary action in the deltoid and pectoral muscles. Sensation has returned as far as the elbow, and there are points over the forearm and hand where the patient has some sensation. The muscles react well to the galvanic current, and the general appearance of the arm is much better. The rapidly returning sensation gives promise of further restoration of function.

There have been four other cases of ruptured brachial plexus in the hospital; the first was recorded in 1892. The patient had a complete rupture of the left brachial plexus. At operation the three main trunks were found encased in a firm, dense, fibrous tissue mass, which it was considered best not to dissect out. Three weeks later at the patient's request the arm was amputated. This was the usual treatment of total brachial plexus ruptures at that time, for the condition was regarded as hopeless, and the flail-like extremity was an encumbrance.

The second case was in 1893; the rupture of the plexus was not complete; the paralysis simulated Erb's type; the two upper cords were most affected. At operation much scar tissue was found around the trunks. After dissecting this away the stump of the posterior root was sutured to the main part of the plexus, but the patient was not benefited by the operation when last heard from.

The third case was in 1903. All cords of the right plexus were ruptured. At operation the scar tissue was found to be very extensive. A portion of the plexus was excised and an anastomosis made. The patient was benefited.

The fourth case in 1904, was similar to the third, only the fibrous tissue was more marked. The operation was extensive, a temporary resection of the clavicle being made. The nerve trunks were completely dissected out and several complex anastomoses were made. The spinal accessory was anastomosed into the upper cord of the plexus. The operation was successful in so far as the patient has already regained use of the upper arm and still continues to improve.

CASE II. VON RECKLINGHAUSEN'S DISEASE.—The patient shown by Mr. Helmholz was a white laborer, aged 19 years. Ever since the patient can remember he has had small patches of soft tissue on his body. The condition for which he was shown began twelve years ago, following a kick on the head by a horse. At this situation a tumor appeared and grew until it involved the whole left side of the head. It was painless. The great deformity brought him to the hospital. So far as he knows there has been one similar condition in the members of his family.

At examination his expression was rather dull and he seemed somewhat simple; he does not read or write. On the left side of his head was a soft, flabby tumor, reaching from the outer canthus back to the occiput and to within 2 cm. of the sagittal suture. The ear was dislocated downward far below its natural position and was folded on itself. The hair over the tumor was scant, coarse, and gray. Over the body were punctate as well as large irregular patches of pigmentation; small, bluish pin-point areas, looking like small bruises; congenital moles; and true fibromata mollusca. The patient was operated upon on November 9, by Dr. Cushing at a neighboring hospital, and a diamond-shaped piece of scalp, including the chief portion of the tumor, was removed from the side of the head above the ear. After removal of this tissue the closure of the wound has drawn the eye and ear back to their normal positions.

Pathologically the tumor removed was a piece of scalp 20 cm. long, 8 cm. wide, and from 1 to 1½ cm. thick. On the

under surface was a nerve on which was a fusiform thickening 4 cm. long and 2 mm. in diameter, having a number of growths the size of millet seed, and with a number of thick fibers that could be traced into the œdematous tissue of the scalp itself. A neuroma which was in the scalp above the ear histologically was found to be full of intertwining bands of nerve fibrils. The sebaceous glands of the scalp were hypertrophied. The lower connective tissue layer of the scalp was composed of many whorls of connective tissue. In the midst of these concentric bands of fibrous tissue were a few nerve fibrils.

Dr. Cushing.—Brachial plexus ruptures are not uncommon in the adult. The lesions are the same as those which occur in the so-called obstetrical palsies in infants. In both instances the injury follows a violent separation of the head and shoulder. Mr. Langnecker's patient was a miner, and his plexus was ruptured by a mass of slate falling on his shoulder and causing extreme lateral flexion of the head.

Concerning the case of von Recklinghausen's disease he said: this plexiform manifestation of the disease is not uncommon, particularly over this cranial site. There have been many cases reported with various degrees of the same lesion. The first case of this type of the disease was reported by Valentine Mott in 1854, under the title of Pachydermatocele. Subsequently Paul Bruns called these tumors Ranken-neurome. In 1882, von Recklinghausen gathered together all the reported cases and made exhaustive studies, since when the disease in all of its various manifestations has been associated with his name. The pigmented patches often appear in the skin fields, representing segmental distribution.

Dr. Barker.—In regard to the case of plexus lesion and nerve anastomosis, has regeneration in the distal ends of the nerves been noticed? There is evidence that regeneration can occur in the peripheral nerves. In 1860, French observers claimed that there was at first degeneration, but after some months distal regeneration. Strobe later claimed that there was peripheral degeneration, but that no regeneration took place. The former theory was retracted, but in the last few years there has again been a leaning toward distal regeneration. If there is no connection between the distal and proximal ends, the distal end again degenerates. Bethe made these observations from work on young animals, but there should be the same tendency in older animals.

Dr. Cushing.—There are changes, doubtless reparative in nature, which occur in the distal ends of severed nerves and which are shown chiefly as a multiplication of the cells of the sheath of Schwann. This process has been regarded by almost all observers as a regenerative one but I do not think that those, who like Bethe have gone so far as to claim that the entire process of regeneration, including the reformation of axis cylinder processes, may take place in the distal segment alone, have proven their claim satisfactorily to all. Langley and Anderson have shown how technical errors not guarded against in Bethe's work, may have led to an erroneous interpretation of many of his experiments. It seems probable that a double process must be at work in the regeneration of a severed nerve fiber—the well recognized peripheral changes and the outgrowing axone from the central cell; the former serving the purpose of a guide to the latter.

Experimental Arteriosclerosis and Myocarditis. Dr. R. M. Pearce, of Albany, N. Y.

The term arteriosclerosis is here used in a tentative way to describe the changes occurring in the aorta of the rabbit as the result of the intravenous injection of adrenalin. The lesions thus produced are not identical with the arteriosclerosis of man but for purposes of experimental study they may perhaps for the present at least be regarded as arteriosclerosis for the rabbit. Previous to Josué's publication describing the production of vascular lesions in the rabbit by the use of adrenalin, all attempts to produce experimentally changes analagous to arteriosclerosis had been unsatisfactory. In the experiments about to be described Josué's methods were followed. A few minims of a one to one thousand solution of adrenalin chloride were injected into an ear vein of a rabbit on alternate days. In some instances considerably larger doses were given. The animals were killed after periods varying from a few days to eight weeks.

The vascular lesions produced were limited to the aorta and exhibited a more or less definite sequence. Rabbits receiving five to six injections showed no gross lesions but, histologically, important changes in the media were evident. These consisted of focal areas of degeneration in which the muscle fibers were destroyed without alteration of the elastica. Later the degeneration was more extensive and involved the greater portion of the middle zone of the media. At this time changes in the elastic tissue appeared; the fibers became swollen, stained irregularly and in some places appeared to be fused together. Special stains showed a small number of minute fat droplets in such areas. After 12 to 15 injections very definite lesions were evident macroscopically. The aorta was more or less distorted in shape, rigid and non-elastic. Irregular dilations alternated with elevated brittle areas of calcification. Distinct atheroma with ulceration was seldom seen. In the experiments, continued for six to eight weeks, the process became very diffuse and small dilations of the thinner portions of the aorta assumed the appearance of aneurysms. At this stage the destruction of the elastic fibers was extreme and all degenerated areas were infiltrated with lime salts. Cellular infiltration and repair about such areas were frequently seen in the late stages. In such there was also an extensive proliferation of the sub-intimal tissue. The aorta of the rabbit is a very delicate structure showing no sharp demarcation between the intima and the beginning of the media. There is no definite internal elastic plate and the endothelial cells are separated from the media only by a delicate layer, often not demonstrable, of fine elastic and connective tissue fibrils. In the proliferation in this part of the vessel it is difficult to differentiate between the part played by intimal and sub-intimal tissues. Certain it is that the endothelial cells proliferate not at all or to but a very slight

extent. The proliferation of the intimal and sub-intimal tissue is always opposite areas of necrosis in the media and appear to be compensatory to such and is therefore of unusual interest in view of Thoma's well known theory concerning the development of arteriosclerosis in man. According to Thoma's view the most characteristic lesion of arteriosclerosis is a thickening of the intima compensatory to a weakening of the media. The condition in man is one acting slowly and over a long time. The experimental condition in the rabbit, although more acute and as far as the necrosis is concerned, more severe, is somewhat similar to the slighter changes which occur in man. A secondary degeneration taking place in the areas of compensatory hyperplasia is necessary, however, to make the condition more nearly analagous to arteriosclerosis in man.

The manner in which adrenalin produces these lesions has caused much discussion. Toxic action, the effect of increase of blood pressure and the part played by the vasa vasorum have all been considered. No unanimity of opinion exists. K. Ziegler has pointed out that owing to anatomical peculiarities certain portions of the inner and middle parts of the media of the aorta are not so well nourished as are the other portions and that therefore in such places the toxic substances more readily cause destruction. Although this theory may explain more or less the peculiar distribution of the lesion, it is not entirely satisfactory. It would appear much more probable that the disturbance of circulation is sufficient without a direct toxic action. At the time of arterial contraction caused by the action of adrenalin on the vasa vasorum a condition of local anæmia must exist; if to this we add the great strain on the vessel wall due to the greatly increased intravascular pressure, we have sufficient explanation it would appear for the disorganization of the media.

In the series of experiments just described, which were carried out with the aid of Dr. E. MacD. Stanton, little attention was paid to the condition of the heart. Certain degenerative and proliferative changes were, however, occasionally observed and in order to determine the significance of these a second series of observations was undertaken.

In this second series of thirty-one experiments, degenerative changes in the myocardium were found frequently and connective tissue proliferation of greater or less degree in twelve. The primary effect of adrenalin is to produce severe circulatory disturbances. The animals generally recover from these though some die from extreme dilatation of the heart after one to five injections. In such, disorganization and degenerative changes are constant. Very frequently there is a marked œdema of the myocardium. In those having had four or five injections, areas of granular and hyaline degeneration of the fibers with complete loss of nuclei, a condition practically of anæmic infarction, were not infrequently present. Of twenty-two animals surviving seven to fifteen injections (initial dose of 0.1 cc. gradually increased every other day), twelve exhibited connective tissue proliferation of varying degree. In two the histological picture was that of a chronic fibrous myocarditis. The increase of connective tissue was partly diffuse and partly focal affecting all parts of the ventricle and to a considerable extent the papillary muscles. The focal areas were most frequent at the apex of the heart. As a rule extreme degeneration of muscle and proliferation of connective tissue occurred side by side.

The changes in the myocardium are not secondary to the changes in the aorta for in about half the animals very severe lesions in the heart were unaccompanied by vascular changes. In only one instance did vascular lesions involve the orifices of the coronary arteries. The theory put forth to explain the necrosis in the aorta would appear to be applicable also to the degenerative changes in the myocardium. The fibrous myocarditis represents an attempt to repair the degenerative lesion.

The conditions thus produced experimentally may not be the same as those occurring in man but work along these lines may eventually aid in elucidating some of the problems of vascular and cardiac pathology.

NOTES ON NEW BOOKS.

Operative Surgery. For Students and Practitioners. By JOHN J. MCGRATH, M. D., Professor of Surgical Anatomy and Operative Surgery at the New York Post-Graduate Medical School, Surgeon to the Harlem, Post-Graduate, and Columbus Hospitals, New York. Second edition, thoroughly revised, with 265 illustrations, including many full-page plates in colors and half-tone. (*Philadelphia: F. A. Davis Company, 1906.*)

The first edition of this book was published in 1902, under the title, Surgical Anatomy and Operative Surgery. The present volume is somewhat more voluminous than the first, and there are more and better illustrations.

Among the subjects not considered in the other edition, but now described, are operations for goitre and on the heart. There is still no mention of operations on the ureters, for aneurysm, for umbilical hernia, and others equally important. Some of the sections are practically unchanged, while others have been added to and improved. This is especially noticeable in the section which deals with the stomach and intestines, where many of the latest methods are considered. The original Halsted operation for the radical cure of inguinal hernia is given, and not the modified method now used. Although the book is considerably improved in many respects, it is still incomplete and unsatisfactory.

A Text-Book of Clinical Anatomy for Students and Practitioners. By DANIEL N. EISENDRATH, A. B., M. D., Professor of Clinical Anatomy, University of Illinois. (*Philadelphia, New York, and London: W. B. Saunders & Co.*)

This is a useful book and deserves to be in the hands of every student of medicine, surgeon, and general practitioner. It aims to supplement the study of gross and minute anatomy by giving a view of regional and topographic anatomy to the end that the various anatomical structures may be recognized in the living

body. Directions are given for the various examinations required for purposes of accurate diagnosis. The diagnostic landmarks in different portions of the body are pointed out not only in the text but also by sections and schematic representations. The illustrations are numerous and of excellent quality and serve to elucidate the text and to render the meaning of the author more easily comprehended. The character of the book forbids an extended review of its contents. It is sufficient to say that the work bears evidence throughout of painstaking original work and can be commended as an excellent guide to all who have to do with surgery, neurology, or internal medicine.

Die Morphologie der Missbildungen des Menschen und der Thiere. Part I. *General Teratology.* By Dr. Ernst Schwalbe. (*Jena: Gustav Fischer, 1906.*)

This is the first volume of a text-book which the author has designed to be made up of three parts, the first dealing with general teratology, the second with twin and multiple formations, and the third with individual malformations. The last two volumes have not yet appeared; the first, which is here under consideration, is largely concerned with a discussion of the general conditions which bring about abnormal development.

The brief account which is given of the early literature and the history of monstrosities indicates the extreme ignorance which existed even as late as the seventeenth and eighteenth centuries concerning the cause of abnormal organisms. It was not until embryology became a well-established field of work, that rational studies were made of malformations; and the further development of experimental embryology gave finally an exact basis for what was called the science of teratology.

In Chapter IV the author gives a general review of experimental work which has been done in embryology and teratology, at the basis of which is the fact that the normal development of the egg is dependent upon certain definite external physical and chemical conditions and upon internal conditions of nutrition and assimilation. He cites Boveri's experiments in the production of abnormal larvæ from fragments of the ascaris egg in which there is an abnormally small number of chromosomes; and also the formation of monstrosities by double fertilization in which there is an increase of chromosomes. Among the external conditions which may cause abnormal development are changes in temperature and changes in the oxygen supply, especially lack of oxygen. Definite malformations occur in hens' eggs when the supply of oxygen is diminished. A change in osmotic pressure may cause abnormal development as shown in Loeb's production of artificial parthenogenesis in eggs which have been in concentrated sea water. Certain chemical changes in the surrounding media are of importance; abnormalities develop in calcium-free media, in solutions of lithium salts, etc. The lack of light retards development in frogs' eggs; and the regeneration of organs is also influenced by light. Gravity also has some influence on the development of a hen's egg.

The phenomena of regeneration in the various classes of animals are dealt with in considerable detail. Regeneration may be of all degrees of completeness, depending upon the species of animals and upon local conditions. On the other hand "superregeneration" may take place when the regeneration is greater than the loss, *e. g.*, lizards may grow two or more tails in the place of one which is lost. This is interesting in connection with the occurrence of polydactylous individuals. In relation to teratology, the heteromorphosis of Loeb is perhaps of special significance. The formation of a head in the place of a lost tail on tubularians and similar occurrences in other classes of animals suggest the possibility of this process playing a rôle in the production of monstrosities.

The special physiology of monstrosities depends largely upon the nature of the malformation. With many of these, intrauterine life is possible when extrauterine life is not. The great variety of malformations which may occur in the organs makes a corresponding diversity in physiological properties in the organism.

The period at which the malformation may originate in the life of the organism varies from the time of fertilization of the egg up to the time of birth. Malformations due to arrested development may occur also after birth. Various processes, such as abnormal fusion of organs, splitting of organs, hypertrophy and atrophy, degeneration of tissues, and inflammation may lead to malformations. The causes of malformations are discussed in further detail in Chapter X, where they are classified as mechanical, psychical, physical, and chemical, those due to fœtal disease or retardation of development, and amniotic malformations. A short account of the frequency, sex, and distribution of malformations completes this excellent volume, a notable feature of which is the application of the later results of biological experiment to the study of teratology. The great light which is thrown upon this subject by biological research is apparent in every part of the volume and we look forward with interest to the parts of this book which are yet to be published. J. B. MacCallum.

Therapeutics: Its Principles and Practice. By Horatio C. Wood, M. D., LL. D., and Horatio C. Wood, Jr., M. D. Twelfth edition. (*Philadelphia and London: J. B. Lippincott Company, 1905.*)

A Text-Book of Practical Therapeutics. By Hobart Amory Hare, M. D., B. Sc. Eleventh edition. (*Philadelphia and New York: Lea Brothers & Co., 1905.*)

Organotherapy, or Treatment by Means of Preparations of Various Organs. By H. Batty Shaw, M. D., F. R. C. P. (*Chicago: W. T. Keener & Co., 1905.*)

Of works on therapeutics we have no lack, and the recent revision of the pharmacopeia has resulted in the necessity for new editions of the older books. The works written by Wood and Hare may probably be regarded as the most representative of American treatises on this subject. There are others which deal rather more with pharmacology and materia medica, but these two are essentially concerned with the subject of treatment. The attitude of the profession towards therapeutics has undergone some changes, but there are many of us who still believe that in too many cases treatment is regarded as meaning only the administration of drugs and not the supervision of many other things. We find in Dr. Wood's work that while 812 pages are devoted to the consideration of drugs only 59 are given to general measures, and 20 of these are concerned with electricity. This does not seem to us a proper division of space, too much attention being given to drugs and too little to other measures.

In Dr. Wood's book there is very slight consideration of massage, feeding, the employment of heat and cold, etc. The discussion of drugs is given under the headings of various classes, such as diuretics, alteratives, etc. Every one knows how difficult it is to classify all drugs under given headings, but this seems thus far perhaps the most satisfactory method. It is impossible to review such a work as this in detail and it may be said that as a rule the text is good. There are very full notes from the literature regarding many points and at the end of each section a good bibliography is given. Just by chance we selected the section on Jaborandi for examination. The discussion of this was rather disappointing as there is no mention whatever of the dangers of giving pilocarpine hypodermically. One cannot expect a writer to note every point but this seems one that should be discussed. The danger from pilocarpine is by no means slight but no reference is made to it.

The work of Hare is arranged in quite a different way, being divided into four parts, the first dealing with general considera-

tions, the second with drugs, the third with measures other than drugs, and the fourth with the treatment of special diseases. Taking the space devoted to therapeutic measures we find 406 pages given to drugs and 94 to other procedures and feeding. As already remarked, the disproportion between these two should not be so great. In the discussion of the drugs they are considered alphabetically, which is perhaps in some ways the easiest method. In the section on pilocarpine the same criticism may be applied as was passed on the corresponding section in Dr. Wood's work. The discussion of remedial measures other than drugs is very good, but as already said there is hardly enough of it. In the section on diseases Dr. Hare again simply makes an alphabetical classification, which cannot be regarded as very satisfactory, although it is probably difficult to consider all the diseases of one system together. There is an elaborate index of diseases and remedies.

Dr. Shaw in his work takes up the subject of treatment by preparations of various organs. He has given us as satisfactory a work as the nature of his subject would permit, each organ being taken up separately and after a preliminary note of its anatomy and physiology the pathology and therapeutics are discussed. As might be expected the largest space is given to the discussion of the thyroid gland. It must be confessed that thus far we have not obtained the therapeutic results from the use of gland extracts which were expected. It is, however, probable that more may come out of it in the future, and if we have nothing more than the use of thyroid extract and adrenalin there is much to be thankful for. This work can be recommended as an excellent one for those who desire to obtain a good summary of this subject.

The Diagnosis of Diseases of Women. A Treatise for Students and Practitioners. By PALMER FINDLEY, B. S., M. D., Assistant Professor of Gynecology and Obstetrics, Rush Medical College. Second edition, illustrated. (*Philadelphia and New York: Lea Brothers & Co., 1905.*)

The appearance of a second edition of this work in two years from the publication of the first, indicates that it fills a place in the library of medical text-books. It covers the whole subject indicated in its title from the point of view of clinical manifestations and of gross and microscopic anatomy. Thoroughness is well carried out in all the chapters. Beginning with clinical history, it takes up different methods of examination, devoting separate chapters to the more common instruments used in diagnosis. Chloroform is preferred as an anæsthetic for curettage. This is contrary to the opinion of many surgeons and seems to add unnecessary risk to a slight operation. The chapter on microscopic examination of scrapings and excised pieces is useful and well written, giving a few good methods of preparing tissue for such examination. New chapters on blood examination and bacteriology are introduced on account of the importance of these subjects. The chapter on the blood is too brief for physicians not used to the methods described, and unnecessarily long for one familiar with blood examination. The plates of blood smears are good, but should give stains and magnification or be omitted. The chapter on bacteriology closes the general considerations. The diagnosis of uterine pregnancy is discussed fully. Extrauterine pregnancy receives the careful attention its frequency and importance demand. Chorio-epithelioma malignum, a subject as yet little understood, is treated in accord with the most recent views. An effort has been made to bring everything up to date. The diseases of the external and internal genitalia are taken up in order and discussed at length. While the cell-inclusion theory of the origin of ovarian dermoids receives careful description, no reference is made to the more recent contributions suggesting the ovulogenous origin of such tumors. The conditions, pelvic peritonitis, perimetritis, and parametritis are described, and the points of difference noted; but the author says: "The distinction between perimetritis and parametritis is at all times difficult; . . . . it is to be remembered they can exist together." It seems hardly worth while to cling to the old nomenclature.

The book closes with chapters on diseases of the urethra, bladder, ureters, and kidneys.

The general make-up of the book is excellent; there are, however, a few typographical errors, as in the legends of Plates XLI and XLII. Clearness of description is sometimes wanting. The book has, however, much to commend it. It is profusely illustrated and well indexed.

The Treatment of Diseases of the Eye. By VICTOR HANKE, First Assistant in the University Eye Clinic of Professor E. Fuchs in Vienna. Translated by J. HERBERT PARSONS, B. S., F. R. C. S., Assistant Ophthalmic Surgeon, University College Hospital, London, and GEORGE COATS, M. D., F. R. C. S., Chief Clinical Assistant, Royal London (Moorefields) Ophthalmic Hospital. (*Chicago: W. T. Keener & Co., 90 Wabash Avenue; London: Hodder & Stoughton, 1905.*)

This interesting volume of a little over two hundred pages will be found useful by the general practitioner. There are not a few works of exactly this character which are to be had nowadays, but Hanke's contribution holds its own with the best. At first sight one might be apt to regard it as more of a medical dictionary of the eye than a work which would be useful in the practice of ophthalmology, but a closer perusal shows that it is full of detailed and practical advice which emanates from no less a personage than Fuchs of Vienna. The book simply tells "what we do in the Royal Eye Clinic in Vienna," and it might justly bear this title. The chapter on the cornea will probably be found the most valuable. The cornea always brings out the best in writers of text-books on ophthalmology. We note that dionin is a favorite remedy in various forms of keratitis and we are convinced of its value in the more obscure forms in which the deeper parts are involved. Coming from such a source we look upon the work as trustworthy, a point of view which is strengthened by the fact that it is translated and presented to the English-speaking public by one of the leaders of British ophthalmology.

Surgical Aspects of Digestive Disorders. By JAMES G. MUMFORD, M. D., Visiting Surgeon Massachusetts General Hospital and Instructor in Surgery in the Harvard Medical School, in association with ARTHUR K. STONE, M. D., Physician to Out-Patients, Massachusetts General Hospital and Assistant in the Theory and Practice of Physic in the Harvard Medical School. (*New York: The MacMillan Company, 1905.*)

This volume of 390 pages written by a surgeon and an internist, contains a great mass of interesting information. This association has enabled the authors to arrive at certain broad conclusions which we think are in the main justifiable.

Considerably over one-half of the work is devoted to diseases of the stomach and duodenum which are treated together. The conditions discussed are dilatation, ulcer, and carcinoma, with their diagnosis and medical and surgical treatment.

Short chapters follow on diseases of the gall passages, pancreas, and appendix vermiformis. Abdominal ptosis is also treated.

In addition to the above, the volume contains an appendix by Henry F. Hews, M. D., upon the diagnosis of gastric diseases including the ordinary methods of gastric juice analysis.

The authors do not think that diseases of the bile passages and gastric ulcer are purely surgical affections like appendicitis, but may become so in many instances, and they insist "that in all prolonged or severe disorders of such a nature the views of a properly qualified surgeon should be sought."

We are glad to see this recommendation emphasized but are

disappointed to find no mention of it in certain diseases of the ileum and large bowel, for example, perforation of the bowel in typhoid fever, in which condition a similar association should be as close if not closer.

The work should constitute a connecting link between the views of internists and surgeons as to the subject discussed, and is a valuable contribution. The publishers have done their work well and the illustrations, although few in number, are excellent.

Progressive Medicine. A quarterly digest of advances, discoveries, and improvements in the medical and surgical sciences. Edited by HOBART A. HARE, M. D., Professor of Therapeutics and materia medica in the Jefferson Medical College, Philadelphia, etc., assisted by H. R. M. LANDIS, M. D., Demonstrator of Clinical Medicine in the Jefferson Medical College. Vol. III, September, 1905. (*Philadelphia and New York: Lea Brothers & Co.*)

This number contains a very good and complete review of the recent work on obstetrics, about one-third of the volume being devoted to that branch of medicine. There is, however, no marked advance in our knowledge of the subject.

A new classification of hyperemesis gravidarum is given by Williams and a method of differential diagnosis between the toxæmic and other forms. He divides the cases into the neurotic, reflex, and toxæmic, and shows that the ammonia output in the urine is normal in the first two and high in the third form, and advises induction of abortion when the ammonia coefficient is above ten per cent.

The section on artificial dilatation of the cervix gives the preference to instrumental methods for rapid dilatation, though a number of writers advocate vaginal cæsarean section. The combination of metal dilators and bags is advocated when the conditions are such that it is not necessary to complete the emptying of the uterus for several hours.

Van de Velde reports on several cases of hebotomy or extramedian symphysiotomy with very good results, and claims that this operation causes a permanent increase in the size of the pelvis.

There are several interesting and unusual cases reported.

The arrangement of the subjects under the headings pregnancy, labor, the puerperium, and obstetric surgery is very good.

At times it is difficult to tell from whom the author is quoting and one often needs to read several paragraphs before this point can be determined, and again there is sometimes confusion as to whether the author's or another's views are being given.

The Diagnostics of Internal Medicine. By G. R. BUTLER, Sc. D., M. D. Second revised edition. (*New York and London: D. Appleton & Co., 1905.*)

This is a very useful, compact work on medical diagnosis. Preceding the body of the text is a schedule for physical examination. The book proper is divided into two parts. The first, "The Evidences of Disease," comprises the larger portion of the reading matter, in it the various general symptoms are described and their possible causes enumerated; then follows the routine in the examination of the various systems, with a careful, though brief, description of all special physical signs, clinical methods, and instruments that are of aid in diagnosis. The second portion of the work is devoted to "Direct and Differential Diagnosis"; in it the main symptoms and physical signs of each disease are briefly presented, while the chief conditions from which the disease under discussion may be differentiated, are enumerated. There is a liberal use of italics and large type which may help to secure clearness of arrangement and promote ease of reference. Moreover, there is a good index and odd-page headings have been added. The plates are for the most part borrowed from other writers, but the diagrams appear to be original. The latter, though useful, are perhaps a little too realistic in their execution, and may prove too diverting to the average student.

The book, in short, is quite up to date, and will prove of considerable value to the practitioner as well as to the student.

C. P. H.

Sexual Disorders of the Male and Female. By ROBERT W. TAYLOR, A. M., M. D., Consulting Genitourinary Surgeon to Bellevue and to the City (Charity) Hospitals, New York. (*New York and Philadelphia: Lea Brothers & Co., 1905.*)

The new edition of this work contains some added chapters on diseases and lesions of the female genital tract; many other sections have also been much amplified. The results too of the more recent studies of the secretions of the prostate and seminal vesicles have been incorporated.

It is only within very recent years that sexual disorders have been taken from the realm of theory and placed for the most part upon a firm pathological basis. The many, heretofore, so-called sexual diseases we now recognize as being most frequently but symptoms of definite pathological changes in the genital or urogenital tract. Hence, a treatise on sexual disorders resolves itself largely into a consideration of the inflammatory lesions of the urethral and genital tract, and so the author naturally gives considerable space to the subjects of chronic urethritis, prostatitis, etc.

The malformations and deformities, both acquired and congenital of the male genitalia, are gone into in some detail in addition to being well illustrated, while those troubles dependent upon a neuropathic condition receive but passing notice.

The work as a whole is treated in as complete and scientific a manner as the present state of our knowledge permits.

A Text-Book of Diseases of the Nose and Throat. By D. BRADEN KYLE, M. D. Third edition, revised and enlarged. (*Philadelphia, New York, London: W. B. Saunders & Co.*)

The third edition of this work can, on the whole, be recommended to students and practitioners interested in diseases of the nose and throat. We heartily agree with the author in his elimination of the word catarrh to designate inflammation of the mucous membrane, whether acute or chronic. This term is and has been used indiscriminately, not alone by the layman but also by the physician to designate inflammations of the nose and throat in general. As the author states, it is more proper to use a term that describes the existing pathological condition. He has classified these diseases on this basis, with a resulting clear and minute assorting of the various diseases.

The chapters treating of general considerations of mucous membranes and their pathology are highly interesting. The author thinks that by a study of the salivary secretion we can better judge the conditions of the chemical constituents of the system and determine the physiological and pathological processes going on within the body. He opposes all our knowledge of the chemistry of metabolism, when he states that a study of the saliva gives us more knowledge about these processes than an examination of the excretory secretions. He ascribes many diseases of the upper respiratory tract to an altered chemical condition of the saliva. In his discussion of hay fever, he does not even mention Dunbar's serum treatment.

The diseases of the accessory sinuses receives thorough treatment. The relationship of pathological processes of the nose and eye through the lachrymal duct are mentioned but the not infrequent class of eye troubles secondary to disease of the accessory sinuses of the nose is not spoken of. In the discussion of the treatment of deflections of the nasal septum, the author fails to describe the best methods of treatment, namely, the submucous operation as devised by Krieg abroad and Freer in this country.

The publishers deserve credit for the excellent appearance of the book.

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